Remarks

Applicants request reconsideration of the above-referenced patent application.

I. Amendments to Specification

In accordance with 37 CFR §1.78 and MPEP §202.01, a new section has been inserted at the beginning of the specification to identify the patent applications to which this patent application is claiming priority. This language is consistent with Applicants' claims for priority in their Declaration and Power of Attorney.

Applicants have amended the formula on page 361, line 17-19 to replace the thio group with an oxy group. This amendment is supported by the title bridging lines 13-16 on page 361.

Applicants' specification inadvertently labeled both examples on pages 426 and 427 as "Example 59". This Amendment B labels the example on page 427 as "Example 59(b)". The table on page 874 has likewise been amended to indicate that the data listed for example "59" corresponds to the compound of Example 59(b). Dr. McDonald's declaration confirms that the compound of Example 59(b) is the compound corresponding to this data.

In the table on page 874, the data corresponding to the compound of Example 46 has been deleted because there is no Example 46 in Applicants' specification.

In the table on page 874, the intermediate compound of Example 55 was inadvertently listed in column 1 as the compound corresponding to the data of Example 56. This caused the numbering in column 1 to be incorrect for the next 3 compounds as well. This Amendment corrects this error, and is supported by Dr. Joseph McDonald's Declaration (enclosed with this Amendment B).

In the table on page 874, the data corresponding to the compound of Example 62 has been deleted because it is inaccurate. The compound of Example 62 is the same compound as in Example 11. The accurate data for this compound is provided in the table on page 872 for the compound of Example 11.

The data in the table on page 874 corresponding to the compound of Example 66 was inadvertently switched with the data in the table corresponding to the compound of Example 67. The table has been amended to correct this error. In addition, the MMP-13 IC_{50} value corresponding to the compound of Example 67 has been corrected (this corrects an obvious error, given that the 36000 Nm IC_{50} value exceeds the 10000 nM detection limit of the

experimental protocol). The MMP-2 IC_{50} value for Example 67 also has been amended to replace 4590 nM with 9000 nM. Dr. McDonald's declaration supports these amendments.

The text on pages 890 and 891 is repeated on pages 892 and 893. Thus, Applicants have deleted pages 890 and 891 to remove the redundancy.

II. Amendments to the Claims

This Amendment B cancels claims 17-19, 23-25, 29-33, and 72-81; amends claims 7-12, 14, 15, 20-22, 26-28, 35, 41, 42, 52-55, 57-65, 67-71, 82-85, 87-94, and 128-131; and adds new claims 147-161. Thus, claims 7-16, 20-22, 26-28, 35-42, 52-65, 67-71, 82-85, 87-94, 128-131, and 147-161 are pending. The amended and new claims are shown in the previous section, and the corresponding amendments are shown in Appendix A. These amendments do not introduce any new matter:

The claims have been amended to be consistent with Applicants' restriction requirement election. Specifically, claims 7, 15, 20, and 35 have been amended to be directed to treating angiogenesis. This amendment is supported by Applicants' specification at, for example, page 30, line 6; and page 31, lines 1-17. Additionally, in claims 7, 15, 20, 52, and 62, the ring containing X, Y, and Z has been defined such that one of X, Y, and Z is oxygen; the remaining two of X, Y, and Z are $-C(R^8)(R^9)-$ and $-C(R^{10})(R^{11})-$; and the sum of m+n+p has been defined as being 2. And the compounds recited in claims 16, 35, 63, 69, 82, 83, and 87 have been defined as corresponding to a tetrahydropyranyl formula. These amendments are supported by Applicants' specification at, for example, Tables 120-127 on pages 254-261; Example 11 on page 332-335; Example 16 on pages 342-344; Example 20 on pages 350-351; Examples 25 and 26 on pages 359-362; Examples 55-73 on pages 420-446; Examples 94-108 on pages 484-506; Examples 120-232 on pages 520-566; Examples 234-387 on pages 568-610; Examples 446-531 on pages 735-742; Examples 607-634 on pages 761-767; Example 649-668 on pages 773-779; and Example 671 on pages 783-787. New claims 147, 148, 157, and 159, which also recite compounds corresponding to a tetrahydropyranyl formula, are similarly supported.

In claims 7, 12, 15, 20, 52, 57, and 62, the term "heterocycloalkyl" has been replaced with "heterocyclo". This terminology is consistent with the definitions on page 86, lines 4-11.

In claims 7 and 52, the -G-A-R-E-Y substituent has been defined as comprising at least two ring structures. This amendment is supported by Applicants' specification at, for example, page 67, line 6-9.

In claims 7 and 35, the term "cycloalkoxyalkyl" has been replaced with "cycloalkyloxyalkyl". This corrects an obvious typographical error, and is therefore permissible under MPEP §2163.07.

Claims 8, 26, and 53 and have been amended to replace "carbocyclic or heterocyclic rings" with "ring structures independently selected from the group consisting of cycloalkyl, aryl, heterocyclo, and heteroaryl". This amendment is supported by Applicants' specification at, for example, the definitions on page 85, line 27 to page 87, line 1.

Claims 7, 15, 52, and 62 have been amended to replace "heterocyclic" with "heterocyclo". This amendment is supported by Applicants' specification at, for example, page 86, line 4.

Claim 20 has been amended to replace Formula IV with Formula III, and include definitions for R^8, R^9, R^{10}, R^{11}, R^{14}, R^{15}, W, m, n, p, X, Y, and Z. Support for this amendment may be found in Applicants' specification at, for example, page 15, line 7 to page 20, line 2; and page 23, lines 11-21. New claim 158, which recites the same compounds as claim 20 (and salts thereof), is similarly supported.

Claim 20 has been amended to remove the redundant "benzofused heterocycloalkyl" from the definition of R^3. This amendment corrects an obvious error, and is therefore permissible under MPEP §2163.07.

Claims 52, 62, 69, and 87 have been amended to remove the "pharmaceutically acceptable" description of the covered salts. Broadening the scope of the recited salts is supported by Applicants' specification at, for example, page 301, lines 16-18. This text describes uses of salts that would not necessarily require the salts to be pharmaceutically acceptable.

Claims 64, 65, 71 have been amended to define the salts from the which claims 64, 65, and 71 depend as "pharmaceutically acceptable salts." This amendment is supported by Applicants' specification at, for example, page 93, line 27 to page 94, line 20; page 300, lines 14 to page 301, line 15; and claims 52, 62, 69, and 87 (as originally filed). New claims 149-153 and 160 are similarly supported.

Claims 82 and 83 have been amended to make them independent. The compounds recited in these claims are defined as corresponding to a tetrahydropyranyl formula. As noted above, this is supported by Applicants' specification. Claim 83 also has been amended to incorporate the definitions of R^3 and R^{23} from claim 82, *i.e.*, the claim from which claim 83 originally depended.

Claims 128-131 have been amended to include pharmaceutical compositions of pharmaceutically acceptable salts of the recited compounds. This amendment is supported by Applicants' specification at, for example, page 300, line 14 to page 305, line 7. New claims 154, 156, and 161 are similarly supported.

Other amendments correct grammatical and/or obvious errors, or simply rephrase the claims. These amendments are permissible under MPEP §2163.07.

III. Restriction Requirement

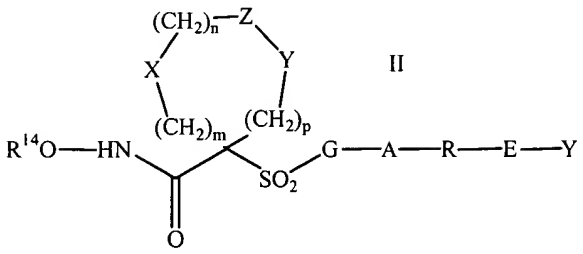
Applicants note that the May 8, 2000 Restriction Requirement defines Group II as having an m+n+p that equals 3. This, however, appears to be an error. After all, according to the Group II definition, the ring between the carbonyl and sulfur is a pyranyl (*i.e.*, a 6-member ring); X, Y, or Z is oxygen; and the remaining two of X, Y, and Z are CR^8R^9 and $CR^{10}R^{11}$. Thus, the sum of m+n+p should be 2 so that the total number of carbons in the ring is 5.

IV. Rejection of claims 7-33, 35-42, 52-65, 67-85, 87-92, 94, and 128-131 under 35 U.S.C. §103 in view of Bender et al.

Claims 7-33, 35-42, 52-65, 67-85, 87-92, 94, and 128-131 have been rejected under 35 U.S.C. §103 in view of Bender et al. (U.S. Patent No. 5,932,595). Claims 17-19, 23-35, 29-33, and 72-81 have been canceled, thereby mooting this rejection as to those claims. As to the remaining pending claims, Applicants request reconsideration of this rejection.

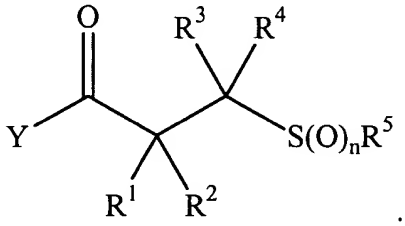
A. Claim 7

Claim 7 is directed to the use of a compound (or salt thereof) to treat a mammal having a condition associated with pathological MMP activity. The compound corresponds in structure to formula II:



Pursuant to Applicants' restriction requirement election, the X-Y-Z ring in the above structure has been restricted to a 6-member ring containing five carbon ring members and one oxygen ring member. As can be seen in Formula II, there is one carbon atom separating the carbonyl from the sulfonyl. In other words, these compounds are "1-carbon compounds". Applicants have observed that an advantage of these compounds is their generally tendency to be potent toward inhibiting MMP-13 (*i.e.*, an MMP believed to be associated with various pathological conditions), while exhibiting substantially less potency toward inhibiting MMP-1 (*i.e.*, an MMP believed to typically be associated with normal body function). See, e.g., Applicants' Specification, page 29, line 23 to page 30, line 17.

In contrast to Applicants' compounds, Bender et al.'s compounds correspond in structure to the following formula:

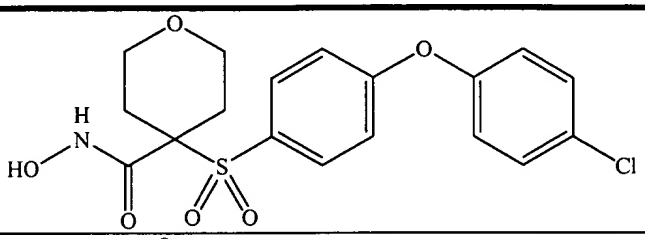
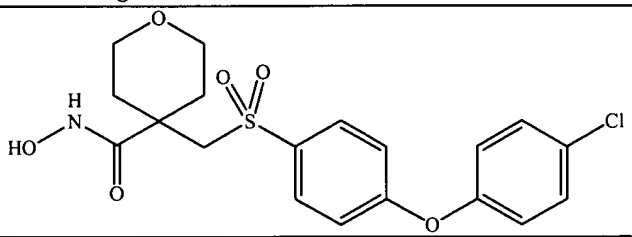
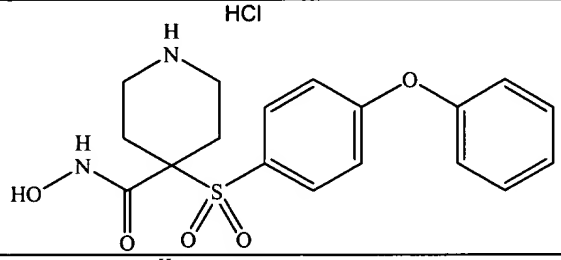
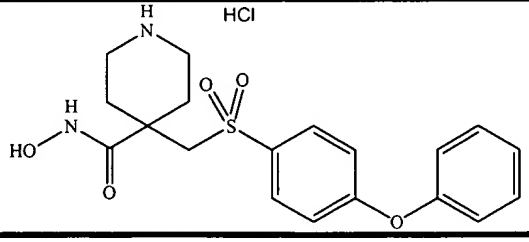


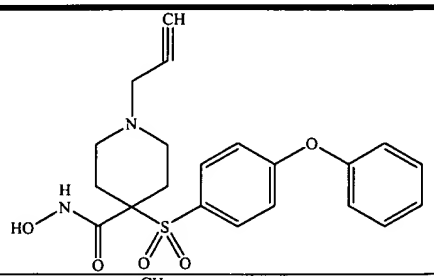
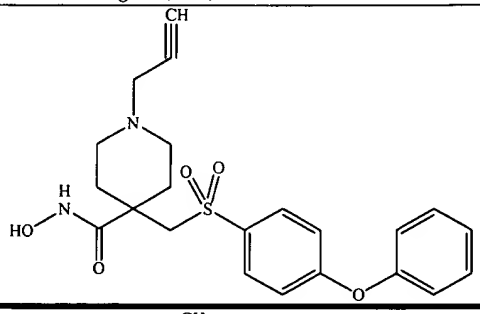
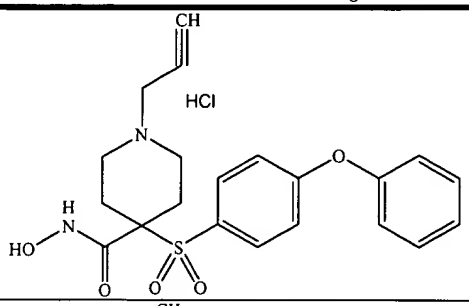
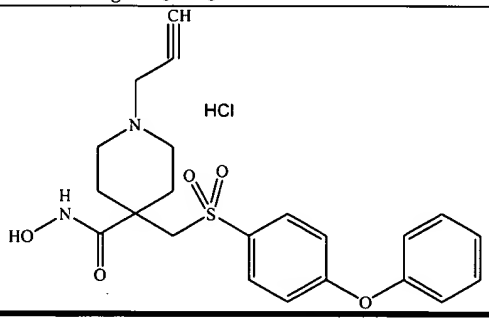
In some of these compounds, n is 2, and either R^1 and R^2 or R^3 and R^4 form a heterocyclo ring. All these compounds, however, have two carbon atoms separating the carbonyl from the sulfonyl. In other words, Bender et al's compounds are "2-carbon compounds".

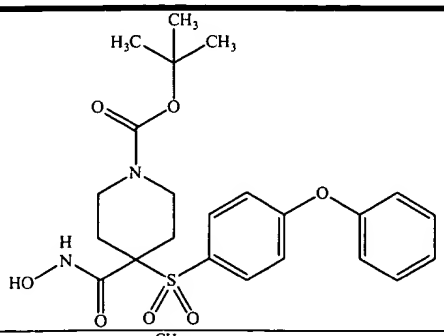
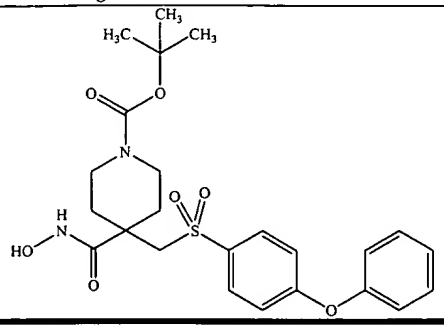
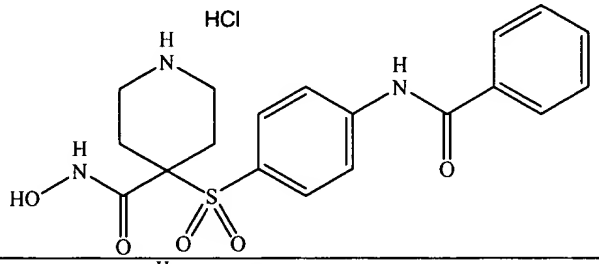
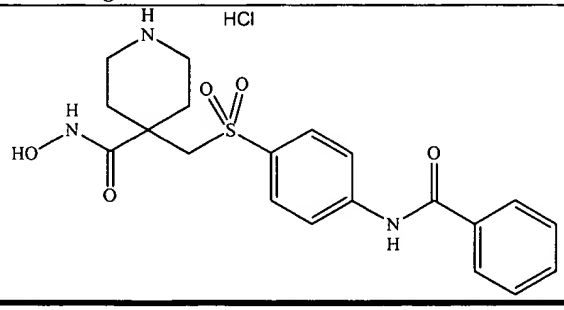
Applicants submit that their 1-carbon compounds and salts are not an obvious variation of Bender et al.'s 2-carbon compounds and salts. Bender et al. fail to teach, suggest, or provide motivation for any 1-carbon compound or salt. Additionally, Applicants have observed that their compounds and salts tend to possess unexpectedly advantageous properties over such 2-carbon compounds and salts. See M.P.E.P. §2144.09 ("A *prima facie* case of obviousness based on structural similarity is rebuttable by proof that the claimed compounds possess unexpectedly advantageous or superior properties"). Specifically, for example, Applicants have observed that

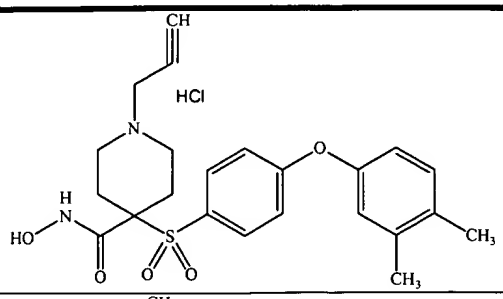
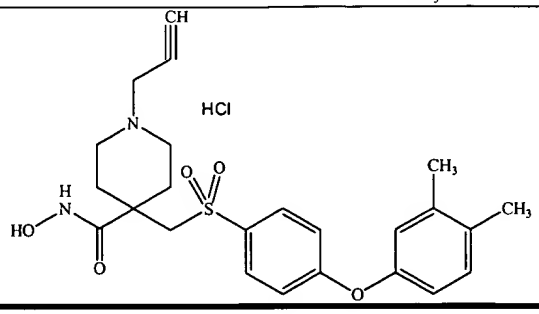
their 1-carbon compounds and salts generally tend to be more potent and/or selective than otherwise identical 2-carbon compounds and salts. This general tendency is demonstrated by the following comparisons from Dr. McDonald's Declaration:

Comparison Between 1-Carbon and 2-Carbon Compounds

Compound or Salt	MMP-1 IC_{50}	MMP-13 IC_{50}	Selectivity (MMP-1/ MMP-13)
	435	0.15	2900
	800	0.6	1330
HCl 	1060 (average from 3 experiments)	0.33 (average from 3 experiments)	2890 (average from 3 experiments)
HCl 	2400	8.0	300

Compound or Salt	MMP-1 IC_{50}	MMP-13 IC_{50}	Selectivity (MMP-1/ MMP-13)
	327	0.25	1310
	349	0.5	698
	239 (average from 3 experiments)	0.13 (average from 3 experiments)	1770 (average from 3 experiments)
	485	0.6	808

Compound or Salt	MMP-1 IC_{50}	MMP-13 IC_{50}	Selectivity (MMP-1/ MMP-13)
	1140	0.3	3800
	475	0.2	2375
	>10000	24.1	415
	>10000	243	41.1

Compound or Salt	MMP-1 IC_{50}	MMP-13 IC_{50}	Selectivity (MMP-1/ MMP-13)
	7000	0.8	8750
	7700	0.85	9060

The above table compares Applicants' 1-carbon compounds or salts with 2-carbon compounds or salts that are otherwise identical. Dr. McDonald believes that Applicants only have data for one such pair of compounds wherein the carbon linkage between the sulfonyl and carbonyl is substituted with a tetrahydropyranyl group (*i.e.*, compounds falling within Applicants' restriction requirement election). Applicants have therefore also included data in the above table for 6 pairs of compounds or salts wherein the carbon linkage is substituted with a piperidinyl group.

As can be seen by the above comparisons, the length of the carbon linkage between the sulfonyl and the carbonyl unexpectedly tended to affect the potency and selectivity of the compounds. Six out of the seven 1-carbon compounds or salts exhibited greater potency and/or selectivity when compared to otherwise identical 2-carbon compounds or salts. Given, for example, this unexpected advantage, Applicants' 1-carbon compounds and salts cannot be obvious in view of Bender et al.'s 2-carbon compounds and salts. The obviousness rejection of claim 7 in view of Bender et al. must therefore be withdrawn.

B. <u>Claims 8-16, 20-22, 26-28, 35-42, 52-65, 67-71, 82-85, 87-92, 94, 128-131, and 147-161</u>

All the remaining pending rejected claims and new claims (*i.e.*, claims 8-16, 20-22, 26-28, 35-42, 52-65, 67-71, 82-85, 87-92, 94, 128-131, and 147-161) are directed to 1-carbon

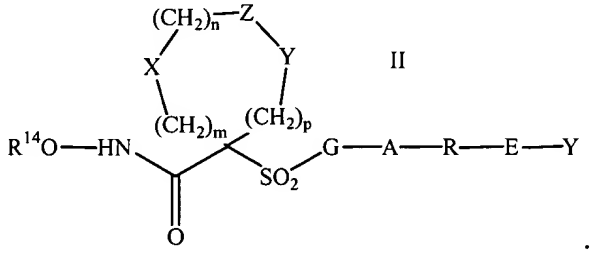
compounds and salts, the use of such compounds and salts, and pharmaceutical compositions comprising such compounds and salts. Thus, these claims are patentable over Bender et al. for the same reasons as stated above with respect to claim 7, and by reason of the additional limitations that claims 8-16, 20-22, 26-28, 35-42, 52-65, 67-71, 82-85, 87-92, 94, 128-131, and 147-161 recite.

V. Rejection of claims 7-33, 35-42, 52-85, 87-92, and 128-131 under 35 U.S.C. §103 in view of Venkatesan et al.

Claims 7-33, 35-42, 52-85, 87-92, and 128-131 have been rejected under 35 U.S.C. §103 in view of Venkatesan et al. (WIPO Int'l Publ. No. WO 98/37877). Claims 17-19, 23-35, 29-33, 66, and 72-81 have been canceled, thereby mooting this rejection as to those claims. As to the remaining pending claims, Applicants request reconsideration of this rejection.

A. Claim 7

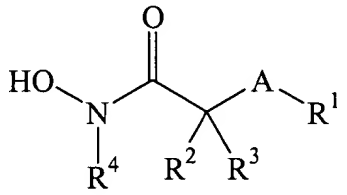
As noted above, claim 7 is directed to the use of compounds (and salts thereof) corresponding in structure to formula II:



In these compounds and salts, the -G-A-R-E-Y substituent comprises at least two ring structures. Applicants have observed that the length of the -G-A-R-E-Y substituent unexpectedly tends to play a role in the overall MMP inhibition activity of a compound, as well as the selectivity of the compound toward MMPs (*e.g.*, MMP-2, MMP-9, and/or MMP-13) typically associated with pathological conditions over MMPs (*e.g.*, MMP-1) necessary or desirable for normal body function. In particular, Applicants have observed that a multi-ring -G-A-R-E-Y substituent (like the -G-A-R-E-Y substituent in claim 7) tends to enhance the potency and selectivity relative to a single-ring -G-A-R-E-Y substituent. See, e.g., Applicants' specification, page 67, lines 6-9. This tendency is evidenced by comparing the inhibition and selectivity data in the tables attached to this Amendment B as Appendix B. The compounds in the first table are tetrahydropyranyl

compounds wherein the substituent on the sulfonyl contains a single ring. The compounds in the second table are tetrahydropyranyl compounds wherein the substituent on the sulfonyl is a multi-ring substituent. As can be seen, the compounds that have a multi-ring substituent generally tended to be more potent and/or selective than the compounds having a single-ring substituent.

Venkatesan et al. disclose a wide variety of compounds that reportedly inhibit MMP activity and correspond in structure to the following formula:



Here, A is -S-, -S(O)-, or -$S(O)_2$-. R^2 and R^3 (together with the carbon to which they are bonded) form a heterocyclic ring. R^1 is defined as a wide range of both cyclic and non-cyclic substituents, which, in turn, can be substituted with one or two R^5 substituents that are defined as being a wide range of cyclic and non-cyclic substituents. See Venkatesan et al., page 3, line 13 to page 11, line 31. Venkatesan et al. also provide a list of 27 compounds that Venkatesan et al. purport to be the most preferred compounds. In all those compounds (and in contrast to claim 7), R^2 and R^3 form piperidinyl, and R^1 is methoxyphenyl or butoxyphenyl. See Venkatesan et al., page 11, line 33 to page 13, line 12; and Examples 83-109, page 82, line 6 to page 105, line 34.

Venkatesan et al. would have failed to teach, suggest, or provide motivation to one of ordinary skill in the art to select a tetrahydropyranyl compound or salt satisfying the multi-ring definition for -G-A-R-E-Y in claim 7. More specifically, Venkatesan et al. disclose a very large genus of compounds. For such a genus to support a prima facie showing of obviousness, Venkatesan et al. would have to provide motivation to specifically select a compound of claim 7 over compounds from that genus. As stated in MPEP §2144.08:

> Office personnel should determine whether one of ordinary skilled in the art would have been motivated to make the claimed invention as a whole, *i.e.*, to select the claimed species or subgenus from the disclosed prior art genus.

(emphasis added). Venkatesan et al. fail to provide any such motivation. Simply put, there is no teaching or suggestion that would have steered one skilled in the art toward making a tetrahydropyranyl compound having a multi-ring -G-A-R-E-Y substituent over making any

compound falling within the genus disclosed by Venkatesan et al. And, in fact, Venkatesan et al. would have steered one skilled in the art away from the -G-A-R-E-Y substituents of claim 7 because Venkatesan et al. expressly point to alkoxyphenyl (rather than a multi-ring substituent) as being the most preferred substituent on the sulfonyl group. See MPEP §2145 ("A prior art reference that 'teaches away' from the claimed invention is a significant factor to be considered in determining obviousness.").

Venkatesan et al. simply failed to recognize any significance in having a multi-ring -G-A-R-E-Y substituent as described in claim 7. Applicants, not Venkatesan et al., recognized that a multi-ring -G-A-R-E-Y substituent tends to be advantageous for activity and/or selectivity. Neither these advantages nor any other motivation is provided by Venkatesan et al. for the multi-ring -G-A-R-E-Y substituents recited in claim 7. Thus, Venkatesan et al. cannot support a prima facie showing of obviousness as to claim 7, and the obviousness rejection must be withdrawn.

B. Claims 8-16, 20-22, 26-28, 35-42, 52-65, 67-71, 82-85, 87-92, 128-131, and 147-161

All the remaining pending rejected claims and new claims (*i.e.*, claims 8-16, 20-22, 26-28, 35-42, 52-65, 67-71, 82-85, 87-92, 128-131, and 147-161) are directed to tetrahydropyranyl compounds and salts having a multi-ring substituent (*i.e.*, -G-A-R-E-Y or R^3) attached to the sulfonyl, the use of such compounds and salts, and pharmaceutical compositions comprising such compounds and salts. Thus, these claims are patentable over Venkatesan et al. for the same reasons as stated above with respect to claim 7, and by reason of the additional limitations that claims 8-16, 20-22, 26-28, 35-42, 52-65, 67-71, 82-85, 87-92, 128-131, and 147-161 recite.

VI. Rejection of claims 7-33, 35-42, 52-65, 67-85, 87-92, 94, and 128-131 under 35 U.S.C. §103 as being unpatentable over Venkatesan et al. in view of Bender et al.

Claims 7-33, 35-42, 52-65, 67-85, 87-92, 94, and 128-131 have been rejected under 35 U.S.C. §103 as being unpatentable over Venkatesan et al. in view of Bender et al. Claims 17-19, 23-35, 29-33, and 72-81 have been canceled, thereby mooting this rejection as to those claims. As to the remaining pending claims, Applicants request reconsideration of this rejection.

A. Claim 7

As discussed above, claim 7 is not obvious in view of either Venkatesan et al. alone or Bender et al. alone. Applicants submit that claim 7 also is not obvious with respect to the combined disclosures of Venkatesan et al. and Bender et al. Specifically, the cited references fail to support a showing of obviousness for at least 2 reasons:

1. Claim 7 is patentable over the cited references because there is no motivation in the cited references to combine their teachings.

A showing of obviousness requires that the references provide motivation to combine their teachings. The mere fact that the references may disclose individual elements that can be combined to form a compound of claim 7 is simply not enough for such a showing --- the references must provide motivation that would have led one skilled in the art to combine those elements. As stated in MPEP §2143.01:

> The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination.

The Office action does not point to any such motivation in the references. And there simply is no such motivation discussed in the cited references.

In addition to not providing any motivation for combining the teachings of the references, the references actually teach away from the compounds and salts of claim 7. Specifically, Bender et al. point only to compounds having a 2-carbon linkage (rather than a 1-carbon linkage) between the carbonyl and sulfonyl. And Venkatesan et al. point to alkoxyphenyl (rather than a multi-ring substituent) as being the most preferred substituent on the sulfonyl group. This teaching away prohibits the references from being combined in an obviousness rejection. See MPEP §2145 ("It is improper to combine references where the references teach away from their combination").

2. Claim 7 is patentable over the cited references because the cited references fail to provide any teaching, suggestion, or motivation to specifically prepare a compound of claim 7 over any compound in the very large genus that would be formed if the disclosures of the cited references were combined.

Even assuming that the references did provide a general motivation to combine their disclosures, they would still fail to support a showing of obviousness. More specifically, if the

teachings of the cited references were combined, an enormous genus would be formed. For such a genus to support a showing of obviousness, the references would have to provide motivation to specifically select a compound of claim 7 from that genus. *See* MPEP §2144.08. The cited references fail to provide any teaching, suggestion, or motivation to specifically select a compound recited in claim 7. Simply put, there is no teaching or suggestion that would have steered one skilled in the art toward making a compound of claim 7 over any compound that possibly could be formed by combining the disclosures of the cited references. If anything, the cited references teach away from the compounds of claim 7, as discussed above. Applicants discovered the compounds recited in claim 7 and their tendency to possess advantageous specificity toward inhibiting MMP-2, MMP-9, and/or MMP-13 over MMP-1. Neither this advantage nor any other motivation is provided in the cited references. Claim 7 therefore is patentable over the cited references.

B. Claims 8-16, 20-22, 26-28, 35-42, 52-65, 67-71, 82-85, 87-92, 94, 128-131, and 147-161

All the remaining pending rejected claims and new claims (*i.e.*, claims 8-16, 20-22, 26-28, 35-42, 52-65, 67-71, 82-85, 87-92, 94, 128-131, and 147-161) are directed to 1-carbon compounds and salts having a multi-ring substituent on the sulfonyl, the use of such compounds and salts, and pharmaceutical compositions comprising such compounds and salts. Thus, these claims are patentable over Venkatesan et al. and Bender et al. for the same reasons as stated above with respect to claim 7, and by reason of the additional limitations that claims 8-16, 20-22, 26-28, 35-42, 52-65, 67-71, 82-85, 87-92, 94, 128-131, and 147-161 recite.

VII. Allowable Subject Matter

The subject matter of claim 93 has been found allowable in Paragraph 5 of the Office action. An objection, however, has been raised to claim 93 for being dependent on a rejected claim. Applicants request that this objection be withdrawn in view of the remarks above regarding claim 87 (*i.e.*, the claim from which claim 93 depends).

Applicants note that claim 153 depends from claim 93, and therefore is necessarily allowable for the same reasons as claim 93. Additionally, claim 154, which is directed to pharmaceutical compositions comprising the compound recited in claim 93 (or a pharmaceutically acceptable salt thereof), also is necessarily allowable.

VIII. Information Disclosure Statement

Applicants request that the Examiner consider the references cited in the Information Disclosure Statement that Applicants submitted on August 23, 2001.

IX. Correspondence Address

As noted in Applicants' June 21, 2001 Associate Power and Notice of Change of Address, all future correspondence for this application should be addressed to:

Dr. Mike Warner, PTO Reg. No. 45,199
Corporate Patent Department
Mail Zone O4E
Pharmacia Corporation
800 N. Lindbergh
St. Louis, Missouri 63167

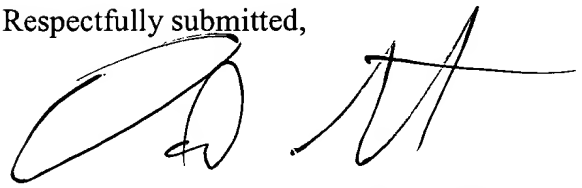
* * * * * * * * *

In view of the foregoing amendments and remarks, Applicants submit that the claims are in condition for allowance.

Applicants also hereby request a 3-month extension pursuant to 37 C.F.R. §1.17 to file this amendment, and have enclosed a check to cover that fee. That check also includes the $372.00 fee for the 15 new claims (including 4 independent claims) and the 2 claims amended to be independent (partially offset by the fee that Applicants have already paid in connection with the 21 claims canceled by this Amendment B). If Applicants have incorrectly calculated these fees, the Commissioner is hereby authorized to charge the deficiency or overpayment to Deposit Account No. **08-0750**. In addition, if there is ever any other fee deficiency or overpayment under 37 C.F.R. §1.16 or 1.17 in connection with this patent application, the Commissioner is hereby authorized to charge such deficiency or overpayment to Deposit Account No. **08-0750**.

The Examiner is requested to call the undersigned if any questions arise that can be handled over the phone to expedite examination of this application.

Respectfully submitted,



David M. Gryte, PTO Reg. No. 41,809
Harness, Dickey & Pierce
Suite 400, 7700 Bonhomme
Clayton, Missouri 63105
(314) 726-7500 (tel)
(314) 726-7501 (fax)

Please send all correspondence to:

Dr. Mike Warner, PTO Reg. No. 45,199
Corporate Patent Department
Mail Zone O4E
Pharmacia Corporation
800 N. Lindbergh
St. Louis, Missouri 63167

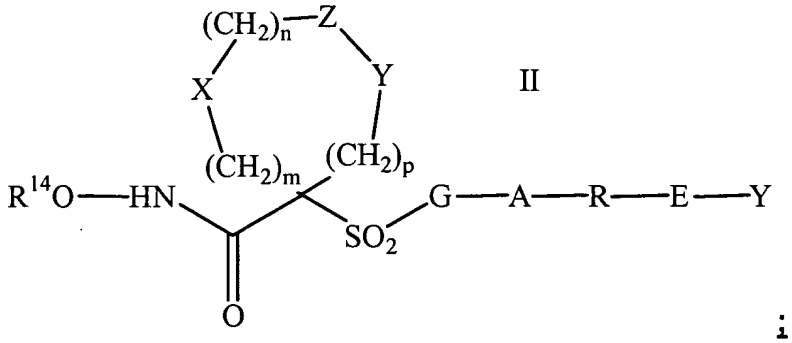
Appendix A
Amendments to Claims

The following amendments were made to the claims by this Amendment B:

7. **(amended once)** A process for treating a host mammal having **[a condition associated with pathological matrix metalloprotease (MMP) activity]** **angiogenesis, wherein:**

the process **[that]** comprises administering a **[metalloprotease inhibitor]** compound or a pharmaceutically acceptable salt thereof in an effective amount to a mammalian host having **angiogenesis, the compound or salt** **[such a condition, said metalloprotease inhibitor]** inhibiting the activity of one or more of MMP-2, MMP-9, and MMP-13, while exhibiting substantially less inhibitory activity against MMP-1; **[, said]**

the compound **corresponds** **[corresponding]** in structure to formula II: **[, below]**



;

[wherein]

R^{14} is hydrido, a pharmaceutically acceptable cation, or $C(W)R^{15}$; **[where]**

W is O or S; **[and]**

R^{15} is selected from the group consisting of **[a]** C_1-C_6-alkyl, aryl, C_1-C_6-alkoxy, heteroaryl-C_1-C_6-alkyl, C_3-C_8-cycloalkyl-C_1-C_6-alkyl, aryloxy, ar-C_1-C_6-alkoxy, ar-C_1-C_6-alkyl, heteroaryl, and amino-C_1-C_6-alkyl, **[group]** wherein the aminoalkyl nitrogen **optionally** is **[(i) unsubstituted or (ii)]** substituted with:

up to **[one or]** two substituents independently selected from the group consisting of **[an]** C_1-C_6-alkyl, aryl, ar-C_1-C_6-alkyl, C_3-C_8-cycloalkyl-C_1-C_6-alkyl, ar-C_1-C_6-

alkoxycarbonyl, C_1-C_6-alkoxycarbonyl, and C_1-C_6-alkanoyl **[radical]**, or **[(iii) wherein the amino C_1-C_6-alkyl nitrogen and]**

two substituents **such that the two substituents, together with the amino-C_1-C_6-alkyl nitrogen, [attached thereto]** form a 5- to 8-membered heterocyclo or heteroaryl ring;

m is zero, 1, or 2;

n is zero, 1, or 2;

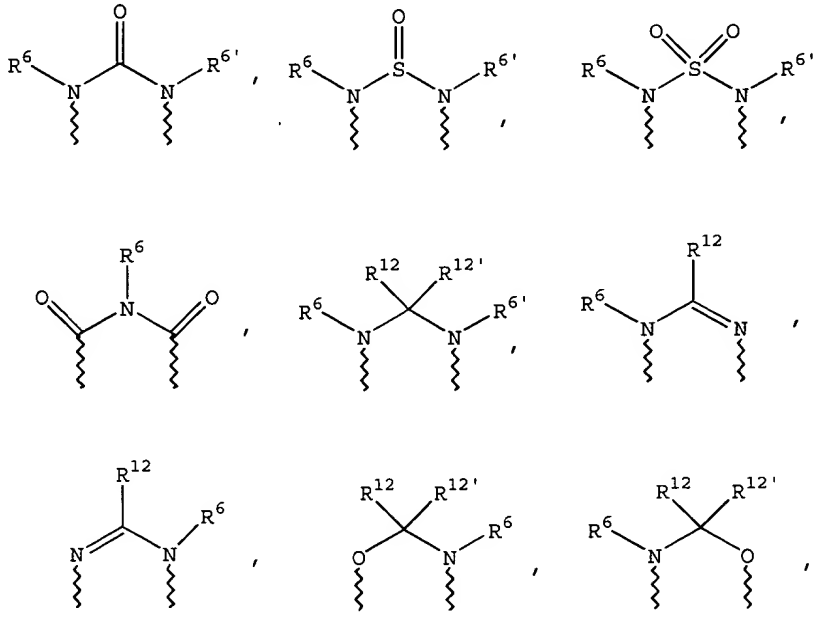
p is zero, 1, or 2;

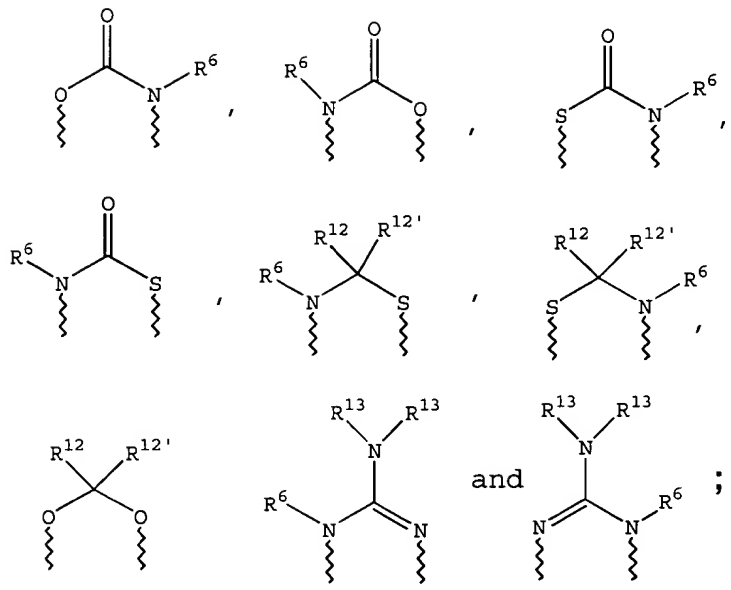
the sum of m + n + p = **[1,]** 2 **[, 3 or 4]**;

[(a)] one of X, Y, and Z is **[selected from the group consisting of C(O), NR^6,]** O, **[S, S(O), $S(O)_2$ and $NS(O)_2R^7$,]** and the remaining two of X, Y, and Z are CR^8R^9 **[,]** and $CR^{10}R^{11}$ **[, or**

(b) X and Z or Z and Y together constitute a moiety that is selected from the group consisting of $NR^6C(O)$, $NR^6S(O)$, $NR^6S(O)_2$, NR^6S, NR^6O, SS, NR^6NR^6, and OC(O), with the remaining one of X, Y and Z being CR^8R^9, or

(c) n is zero and X, Y and Z together constitute a moiety selected from the group consisting of





wherein wavy lines are bonds to the atoms of the depicted ring;

R^6 and $R^{6'}$ are independently selected from the group consisting of hydrido, C_1-C_6-alkanoyl, C_6-aryl-C_1-C_6-alkyl, aroyl, bis(C_1-C_6-alkoxy-C_1-C_6-alkyl)-C_1-C_6-alkyl, C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-perfluoroalkyl, C_1-C_6-trifluoromethylalkyl, C_1-C_6-perfluoroalkoxy-C_1-C_6-alkyl, C_1-C_6-alkoxy-C_1-C_6-alkyl, C_3-C_6-cycloalkyl, C_3-C_8-heterocycloalkyl, C_3-C_8-heterocycloalkylcarbonyl, C_6-aryl, C_5-C_6-heterocyclo, C_5-C_6-heteroaryl, C_3-C_8-cycloalkyl-C_1-C_6-alkyl, C_6-aryloxy-C_1-C_6-alkyl, heteroaryloxy-C_1-C_6-alkyl, heteroaryl-C_1-C_6-alkoxy-C_1-C_6-alkyl, heteroarylthio-C_1-C_6-alkyl, C_6-arylsulfonyl, C_1-C_6-alkylsulfonyl, C_5-C_6-heteroarylsulfonyl, carboxy-C_1-C_6-alkyl, C_1-C_4-alkoxycarbonyl-C_1-C_6-alkyl, aminocarbonyl, C_1-C_6-alkyliminocarbonyl, C_6-aryliminocarbonyl, C_5-C_6-heterocycloiminocarbonyl, C_6-arylthio-C_1-C_6-alkyl, C_1-C_6-alkylthio-C_1-C_6-alkyl, C_6-arylthio-C_3-C_6-alkenyl, C_1-C_4-alkylthio-C_3-C_6-alkenyl, C_5-C_6-heteroaryl-C_1-C_6-alkyl, halo-C_1-C_6-alkanoyl, hydroxy-C_1-C_6-alkanoyl, thiol-C_1-C_6-alkanoyl, C_3-C_6-alkenyl, C_3-C_6-alkynyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, C_1-C_5-alkoxycarbonyl, aryloxycarbonyl, NR^8R^9-C_1-C_5-alkylcarbonyl, hydroxy-C_1-C_5-alkyl, an aminocarbonyl wherein the aminocarbonyl nitrogen is (i) unsubstituted or (ii) substituted

with one or two radicals independently selected from the group consisting of C_1-C_6-alkyl, ar-C_1-C_6-alkyl, C_3-C_8-cycloalkyl and a C_1-C_6-alkanoyl group, hydroxyaminocarbonyl, an aminosulfonyl group wherein the aminosulfonyl nitrogen is (i) unsubstituted or (ii) substituted with one or two radicals independently selected from the group consisting of C_1-C_6-alkyl, ar-C_1-C_6-alkyl, C_3-C_8-cycloalkyl and a C_1-C_6-alkanoyl group, an amino-C_1-C_6-alkylsulfonyl group wherein the amino-C_1-C_6-alkylsulfonyl nitrogen is (i) unsubstituted or (ii) substituted with one or two radicals independently selected from the group consisting of C_1-C_6-alkyl, ar-C_1-C_6-alkyl, C_3-C_8-cycloalkyl and a C_1-C_6-alkanoyl group] and an amino-C_1-C_6-alkyl group, wherein the aminoalkyl nitrogen is (i) unsubstituted or (ii) substituted with one or two radicals independently selected from the group consisting of C_1-C_6-alkyl, ar-C_1-C_6-alkyl, C_3-C_8-cycloalkyl and a C_1-C_6-alkanoyl group;

R^7 is selected from the group consisting of a arylalkyl, aryl, heteroaryl, heterocyclo, C_1-C_6-alkyl, C_3-C_6-alkynyl, C_3-C_6-alkenyl, C_1-C_6-carboxyalkyl and a C_1-C_6-hydroxyalkyl group];

as to R^8:

R^8 **is [and R^9 and R^{10} and R^{11} are independently]** selected from the group consisting of **[a]** hydrido, hydroxy, C_1-C_6-alkyl, C_1-C_6-alkanoyl, aroyl, aryl, ar-C_1-C_6-alkyl, heteroaryl, heteroar-C_1-C_6-alkyl, C_2-C_6-alkynyl, C_2-C_6-alkenyl, thiol-C_1-C_6-alkyl, C_1-C_6-alkylthio-C_1-C_6-alkyl, cycloalkyl, cycloalkyl-C_1-C_6-alkyl, **[heterocycloalkyl-C_1-C_6-alkyl]** **heterocyclo-C_1-C_6-alkyl**, C_1-C_6-alkoxy-C_1-C_6-alkyl, aralkoxy-C_1-C_6-alkyl, C_1-C_6-alkoxy-C_1-C_6-alkoxy-C_1-C_6-alkyl, hydroxy-C_1-C_6-alkyl, hydroxycarbonyl-C_1-C_6-alkyl, hydroxycarbonylar-C_1-C_6-alkyl, aminocarbonyl-C_1-C_6-alkyl, aryloxy-C_1-C_6-alkyl, heteroaryloxy-C_1-C_6-alkyl, arylthio-C_1-C_6-alkyl, heteroarylthio-C_1-C_6-alkyl, **a [the]** sulfoxide **[or sulfone]** of any of said thio substituents, **a sulfone of any said thio substituents,** perfluoro-C_1-C_6-alkyl,

trifluoromethyl-C_1-C_6-alkyl, halo-C_1-C_6-alkyl, alkoxycarbonylamino-C_1-C_6-alkyl, and **[an]** amino-C_1-C_6-alkyl, **[group]** wherein:

the aminoalkyl nitrogen **optionally** is **[(i) unsubstituted or (ii)]** substituted with **up to [one or]** two **substituents [radicals]** independently selected from the group consisting of C_1-C_6-alkyl, ar-C_1-C_6-alkyl, cycloalkyl, and C_1-C_6-alkanoyl, **[or wherein]**

R^8 and R^9, **together with [or R^{10} and R^{11} and]** the carbon to which they are bonded, form a carbonyl group, or **[wherein]**

R^8 and R^9 or **[R^{10} and R^{11}, or]** R^8 and R^{10}, together with the **atom(s) [atoms]** to which they are bonded, form a 5- to 8-membered carbocyclic ring **[,]** or a 5- to 8-membered **[heterocyclic] heterocyclo** or heteroaryl ring **comprising [containing]** one or two heteroatoms **independently selected from the group consisting of [that are]** nitrogen, oxygen, **and [or]** sulfur; **[, with the proviso that]**

as to R^9:

R^9 is selected from the group consisting of hydrido, hydroxy, C_1-C_6-alkyl, C_1-C_6-alkanoyl, aroyl, aryl, ar-C_1-C_6-alkyl, heteroaryl, heteroar-C_1-C_6-alkyl, C_2-C_6-alkynyl, C_2-C_6-alkenyl, thiol-C_1-C_6-alkyl, C_1-C_6-alkylthio-C_1-C_6-alkyl, cycloalkyl, cycloalkyl-C_1-C_6-alkyl, heterocyclo-C_1-C_6-alkyl, C_1-C_6-alkoxy-C_1-C_6-alkyl, aralkoxy-C_1-C_6-alkyl, C_1-C_6-alkoxy-C_1-C_6-alkoxy-C_1-C_6-alkyl, hydroxy-C_1-C_6-alkyl, hydroxycarbonyl-C_1-C_6-alkyl, hydroxycarbonylar-C_1-C_6-alkyl, aminocarbonyl-C_1-C_6-alkyl, aryloxy-C_1-C_6-alkyl, heteroaryloxy-C_1-C_6-alkyl, arylthio-C_1-C_6-alkyl, heteroarylthio-C_1-C_6-alkyl, a sulfoxide of any of said thio substituents, a sulfone of any said thio substituents, perfluoro-C_1-C_6-alkyl, trifluoromethyl-C_1-C_6-alkyl, halo-C_1-C_6-alkyl, alkoxycarbonylamino-C_1-C_6-alkyl, and amino-C_1-C_6-alkyl, wherein:

the aminoalkyl nitrogen optionally is substituted with up to two substituents independently selected from the group consisting of C_1-C_6-alkyl, ar-C_1-C_6-alkyl, cycloalkyl, and C_1-C_6-alkanoyl,

R^9 and R^8, together with the carbon to which they are bonded, form a carbonyl group, a 5- to 8-membered carbocyclic ring, or a 5- to 8-membered heterocyclo or heteroaryl ring comprising one or two heteroatoms independently selected from the group consisting of nitrogen, oxygen, and sulfur;

as to R^{10}:

R^{10} is selected from the group consisting of hydrido, hydroxy, C_1-C_6-alkyl, C_1-C_6-alkanoyl, aroyl, aryl, ar-C_1-C_6-alkyl, heteroaryl, heteroar-C_1-C_6-alkyl, C_2-C_6-alkynyl, C_2-C_6-alkenyl, thiol-C_1-C_6-alkyl, C_1-C_6-alkylthio-C_1-C_6-alkyl, cycloalkyl, cycloalkyl-C_1-C_6-alkyl, heterocyclo-C_1-C_6-alkyl, C_1-C_6-alkoxy-C_1-C_6-alkyl, aralkoxy-C_1-C_6-alkyl, C_1-C_6-alkoxy-C_1-C_6-alkoxy-C_1-C_6-alkyl, hydroxy-C_1-C_6-alkyl, hydroxycarbonyl-C_1-C_6-alkyl, hydroxycarbonylar-C_1-C_6-alkyl, aminocarbonyl-C_1-C_6-alkyl, aryloxy-C_1-C_6-alkyl, heteroaryloxy-C_1-C_6-alkyl, arylthio-C_1-C_6-alkyl, heteroarylthio-C_1-C_6-alkyl, a sulfoxide of any of said thio substituents, a sulfone of any said thio substituents, perfluoro-C_1-C_6-alkyl, trifluoromethyl-C_1-C_6-alkyl, halo-C_1-C_6-alkyl, alkoxycarbonylamino-C_1-C_6-alkyl, and amino-C_1-C_6-alkyl, wherein:

the aminoalkyl nitrogen optionally is substituted with up to two substituents independently selected from the group consisting of C_1-C_6-alkyl, ar-C_1-C_6-alkyl, cycloalkyl, and C_1-C_6-alkanoyl,

R^{10} and R^{11}, together with the carbon to which they are bonded, form a carbonyl group, or

R^{10} and R^8 or R^{10} and R^{11}, together with the atom(s) to which they are bonded, form a 5- to 8-membered carbocyclic ring or a 5- to 8-membered

heterocyclo or heteroaryl ring comprising one or two heteroatoms independently selected from the group consisting of nitrogen, oxygen, and sulfur;

as to R^{11}:

R^{11} is selected from the group consisting of hydrido, hydroxy, C_1-C_6-alkyl, C_1-C_6-alkanoyl, aroyl, aryl, ar-C_1-C_6-alkyl, heteroaryl, heteroar-C_1-C_6-alkyl, C_2-C_6-alkynyl, C_2-C_6-alkenyl, thiol-C_1-C_6-alkyl, C_1-C_6-alkylthio-C_1-C_6-alkyl, cycloalkyl, cycloalkyl-C_1-C_6-alkyl, heterocyclo-C_1-C_6-alkyl, C_1-C_6-alkoxy-C_1-C_6-alkyl, aralkoxy-C_1-C_6-alkyl, C_1-C_6-alkoxy-C_1-C_6-alkoxy-C_1-C_6-alkyl, hydroxy-C_1-C_6-alkyl, hydroxycarbonyl-C_1-C_6-alkyl, hydroxycarbonylar-C_1-C_6-alkyl, aminocarbonyl-C_1-C_6-alkyl, aryloxy-C_1-C_6-alkyl, heteroaryloxy-C_1-C_6-alkyl, arylthio-C_1-C_6-alkyl, heteroarylthio-C_1-C_6-alkyl, a sulfoxide of any of said thio substituents, a sulfone of any said thio substituents, perfluoro-C_1-C_6-alkyl, trifluoromethyl-C_1-C_6-alkyl, halo-C_1-C_6-alkyl, alkoxycarbonylamino-C_1-C_6-alkyl, and amino-C_1-C_6-alkyl, wherein:

the aminoalkyl nitrogen optionally is substituted with up to two substituents independently selected from the group consisting of C_1-C_6-alkyl, ar-C_1-C_6-alkyl, cycloalkyl, and C_1-C_6-alkanoyl,

R^{11} and R^{10}, together with the carbon to which they are bonded, form a carbonyl group, a 5- to 8-membered carbocyclic ring, or a 5- to 8-membered heterocyclo or heteroaryl ring comprising one or two heteroatoms independently selected from the group consisting of nitrogen, oxygen, and sulfur;

only one of R^8 and R^9 or R^{10} and R^{11} is hydroxy;

[R^{12} and $R^{12'}$ are independently selected from the group consisting of a hydrido, C_1-C_6-alkyl, aryl, ar-C_1-C_6-alkyl, heteroaryl, heteroaralkyl, C_2-C_6-alkynyl, C_2-C_6-alkenyl, thiol-C_1-C_6-alkyl, cycloalkyl, cycloalkyl-C_1-C_6-alkyl, heterocycloalkyl-C_1-C_6-alkyl, C_1-C_6-alkoxy-C_1-C_6-alkyl, aryloxy-C_1-C_6-alkyl, amino-C_1-C_6-alkyl, C_1-C_6-alkoxy-C_1-C_6-alkoxy-C_1-C_6-alkyl, hydroxy-C_1-C_6-alkyl, hydroxycarbonyl-C_1-C_6-alkyl,

hydroxycarbonylar-C_1-C_6-alkyl, aminocarbonyl-C_1-C_6-alkyl, aryloxy-C_1-C_6-alkyl, heteroaryloxy-C_1-C_6-alkyl, C_1-C_6-alkylthio-C_1-C_6-alkyl, arylthio-C_1-C_6-alkyl, heteroarylthio-C_1-C_6-alkyl, the sulfoxide or sulfone of any said thio substituents, perfluoro-C_1-C_6-alkyl, trifluoromethyl-C_1-C_6-alkyl, halo-C_1-C_6-alkyl, alkoxycarbonylamino-C_1-C_6-alkyl and an amino-C_1-C_6-alkyl group wherein the aminoalkyl nitrogen is (i) unsubstituted or (ii) substituted with one or two radicals independently selected from the group consisting of C_1-C_6-alkyl, ar-C_1-C_6-alkyl, cycloalkyl and C_1-C_6-alkanoyl;

R^{13} is selected from the group consisting of a hydrido, benzyl, phenyl, C_1-C_6-alkyl, C_2-C_6-alkynyl, C_2-C_6-alkenyl, and a C_1-C_6-hydroxyalkyl group and]

-G-A-R-E-Y is a substituent that:

has a length greater than that of a pentyl group **and** **[has a length that is]** less than that of an icosyl group, **and** **[wherein]**

comprises at least two ring structures;

G is **[an]** aryl or heteroaryl **[group]**;

A is selected from the group consisting of:

(1) –O-, **[;]**

(2) -S-, **[;]**

(3) -NR^{17}-, **[;]**

(4) -CO-N(R^{17})$_2$ **[or]**

(5) -N(R^{17})-CO-, **[wherein R^{17} is hydrogen, C_1-C_4-alkyl, or phenyl;]**

(6) **[(5)]** -CO-O-, **[or]**

(7) -O-CO-, **[;]**

(8) **[(6)]** -O-CO-O-, **[;]**

(9) **[(7)]** -HC=CH-, **[;]**

(10) **[(8)]** -NH-CO-NH-, **[;]**

(11) **[(9)]** -C≡C-, **[;]**

(12) **[(10)]** -NH-CO-O-, **[or]**

(13) -O-CO-NH-, [;]

(14) [(11)] -N=N-, [;]

(15) [(12)] -NH-NH-, [; and]

(16) [(13)] -CS-N(R^{18})-, [or]

(17) -N(R^{18})-CS-, [wherein R^{18} is hydrogen C_1-C_4-alkyl, or phenyl; or]

(18) [(14) A is absent and G is bonded directly to R] a bond;

R^{17} is selected from the group consisting of hydrogen, C_1-C_4-alkyl, and phenyl;

R^{18} is selected from the group consisting of hydrogen, C_1-C_4-alkyl, and phenyl;

R is [a moiety] selected from the group consisting of alkyl, alkoxyalkyl, aryl, heteroaryl, cycloalkyl, [heterocycloalkyl] heterocyclo, aralkyl, heteroaralkyl, [heterocycloalkylalkyl] heterocycloalkyl, cycloalkylalkyl, [cycloalkoxyalkyl] cycloalkyloxyalkyl, heterocycloalkoxyalkyl, aryloxyalkyl, heteroaryloxyalkyl, arylthioalkyl, heteroarylthioalkyl, cycloalkylthioalkyl, and [a heterocycloalkylthioalkyl group] heterocyclothioalkyl, wherein:

the aryl, [or] heteroaryl, [or] cycloalkyl, or [heterocycloalkyl] heterocyclo optionally [substituent] is [(i) unsubstituted or (ii)] substituted with up to [one or] two substituents independently [radicals] selected from the group consisting of [a] halo, alkyl, perfluoroalkyl, perfluoroalkoxy, perfluoroalkylthio, trifluoromethylalkyl, amino, alkoxycarbonylalkyl, alkoxy, C_1-C_2-alkylene-dioxy, hydroxycarbonylalkyl, hydroxycarbonylalkylamino, nitro, hydroxy, hydroxyalkyl, alkanoylamino, and [a] alkoxycarbonyl [group, and R is other than alkyl or alkoxyalkyl when A is -O- or -S-];

E is selected from the group consisting of:

(1) –CO(R^{19})-, [or]

(2) -(R^{19})CO-, [wherein R^{19} is a heterocycloalkyl, or a cycloalkyl group]

(3) [(2)] –CONH-, [or]

(4) -HNCO-, [; and]

(5) [(3)] -CO-, [;]

(6) [(4)] -SO_2-R^{19}-, [or]

(7) $-R^{19}-SO_2-$, [;]

(8) [(5)] $-SO_2-$, [;]

(9) [(6)] $-NH-SO_2-$, [or]

(10) $-SO_2-NH-$, and [; or]

(11) [(7) E is absent and R is bonded directly to Y] a bond; [and]

R^{19} is selected from the group consisting of heterocyclo and cycloalkyl; and

Y is [absent or is] selected from the group consisting of [a] hydrido, alkyl, alkoxy, haloalkyl, aryl, aralkyl, cycloalkyl, heteroaryl, hydroxy, aryloxy, aralkoxy, heteroaryloxy, heteroaralkyl, perfluoroalkoxy, perfluoroalkylthio, trifluoromethylalkyl, alkenyl, [heterocycloalkyl] heterocyclo, cycloalkyl, trifluoromethyl, alkoxycarbonyl, and [a] aminoalkyl [group], wherein:

the aryl, [or] heteroaryl, or heterocyclo optionally [heterocycloalkyl group] is [(i) unsubstituted or (ii)] substituted with up to [one or] two substituents [radicals] independently selected from the group consisting of [an] alkanoyl, halo, nitro, aralkyl, aryl, alkoxy, and [an] amino, [group] wherein:

the amino nitrogen optionally is [(i) unsubstituted or (ii)] substituted with up to [one or] two substituents [groups] independently selected from the group consisting of hydrido, alkyl, and [an] aralkyl [group].

8. **(amended once)** The process according to claim 7, wherein [said] -G-A-R-E-Y [substituent contains] comprises two to four ring structures independently selected from the group consisting of cycloalkyl, aryl, heterocyclo, and heteroaryl [carbocyclic or heterocyclic rings].

9. **(amended once)** The process according to claim 8, wherein each of the two to four ring structures [rings] is 6-membered.

10. **(amended once)** The process according to claim 7, wherein [said] -G-A-R-E-Y [substituent] has a length that is greater than that of a hexyl group and [a length that is] less than that of a stearyl group.

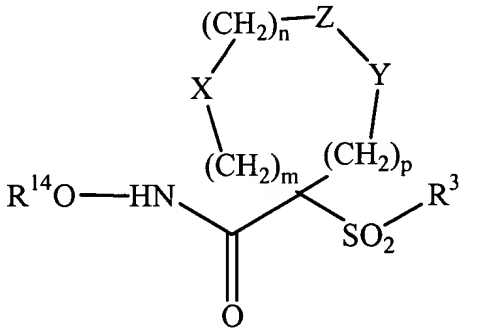
12. **(amended once)** The process according to claim 7, wherein R is **[an]** aryl, heteroaryl, cycloalkyl, or **heterocyclo [heterocycloalkyl group]**.

14. **(amended once)** The process according to claim 7, wherein Y is selected from the group consisting of hydrido, **[an]** alkyl, alkoxy, perfluoroalkoxy, and **[a]** perfluoroalkylthio **[group]**.

15. **(amended once)** A process for treating a host mammal having **[a condition associated with pathological matrix metalloprotease (MMP) activity]** **angiogenesis, wherein:** **[that]**

the process comprises administering a **[metalloprotease inhibitor]** compound or a pharmaceutically acceptable salt thereof in an effective amount to a mammalian host having **angiogenesis, the compound or salt** **[such a condition, said metalloprotease inhibitor]** inhibiting the activity of one or more of MMP-2, MMP-9, and MMP-13, while exhibiting substantially less inhibitory activity against MMP-1; **[, said]**

the compound **corresponds** **[corresponding]** in structure to formula III: **[, below]**



III

;

[wherein]

R^3 is **an** **[a single-ringed]** aryl or heteroaryl group that is 5- or 6-membered **[,]** and **[is itself]** substituted at its own 4-position when a 6-membered ring **or** **[and]** at its own 3- or 4-position when a 5-membered ring with a substituent selected from the group consisting of **[a]** thiophenoxy, 4-chloro-phenoxy, 3-chlorophenoxy, 4-methoxyphenoxy, 3-benzodioxol-5-yloxy, 3,4-dimethylphenoxy, 4-fluorophenoxy, 4-fluorothiophenoxy, phenoxy, 4-trifluoromethoxyphenoxy, 4-trifluoromethylphenoxy, 4-(trifluoromethylthio)phenoxy, 4-

(trifluoromethylthio)thiophenoxy, 4-chloro-3-fluorophenoxy, 4-isopropoxyphenoxy, 4-isopropylphenoxy, (2-methyl-1,3-benzothiazol-5-yl)oxy, 4-(1H-imidazol-1-yl)phenoxy, 4-chloro-3-methylphenoxy, 3-methyl-phenoxy, 4-ethoxyphenoxy, 3,4-difluorophenoxy, 4-chloro-3-methylphenoxy, 4-fluoro-3-chlorophenoxy, 4-(1H-1,2,4-triazol-1-yl)phenoxy, 3,5-difluorophenoxy, 3,4-dichlorophenoxy, 4-cyclopentylphenoxy, 4-bromo-3-methylphenoxy, 4-bromophenoxy, 4-methylthiophenoxy, 4-phenylphenoxy, 4-benzylphenoxy, 6-quinolinyloxy, 4-amino-3-methylphenoxy, 3-methoxyphenoxy, 5,6,7,8-tetrahydro-2-naphthalenyloxy, 3-hydroxymethylphenoxy, and **[a]** 4-benzyloxyphenoxy **[group]**;

R^{14} is hydrido, a pharmaceutically acceptable cation, or $C(W)R^{15}$; **[where]**

W is O or S; **[and]**

R^{15} is selected from the group consisting of **[a]** C_1-C_6-alkyl, aryl, C_1-C_6-alkoxy, heteroaryl-C_1-C_6-alkyl, C_3-C_8-cycloalkyl-C_1-C_6-alkyl, aryloxy, ar-C_1-C_6-alkoxy, ar-C_1-C_6-alkyl, heteroaryl, and amino-C_1-C_6-alkyl, **[group]** wherein the amino-**C_1-C_6**-alkyl nitrogen **optionally** is **[(i) unsubstituted or (ii)]** substituted with:

up to [one or] two substituents independently selected from the group consisting of **[an]** C_1-C_6-alkyl, aryl, ar-C_1-C_6-alkyl, C_3-C_8-cycloalkyl-C_1-C_6-alkyl, ar-C_1-C_6-alkoxycarbonyl, C_1-C_6-alkoxycarbonyl, and C_1-C_6-alkanoyl **[radical]**, or **[(iii) wherein the amino C_1-C_6-alkyl nitrogen and]**

two substituents **such that the two substituents, together with the amino-C_1-C_6-alkyl nitrogen, [attached thereto]** form a 5- to 8-membered heterocyclo or heteroaryl ring;

m is zero, 1, or 2;

n is zero, 1, or 2;

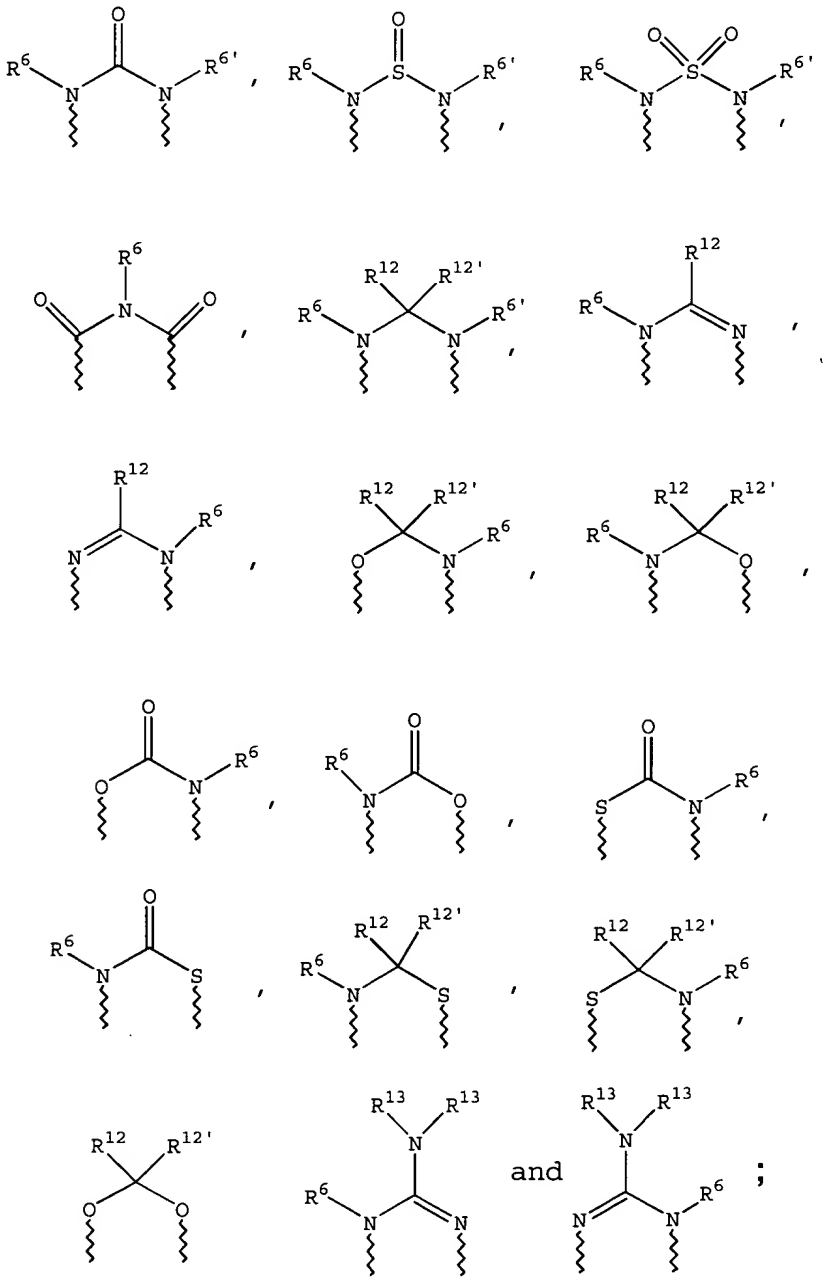
p is zero, 1, or 2;

the sum of m + n + p = **[1,]** 2 **[, 3 or 4]**;

[(a)] one of X, Y, and Z is **[selected from the group consisting of C(O), NR^6,]** O, **[S, S(O), $S(O)_2$, and $NS(O)_2R^7$,]** and the remaining two of X, Y, and Z are CR^8R^9 **[,]** and $CR^{10}R^{11}$ **[, or**

(b) X and Z or Z and Y together constitute a moiety that is selected from the group consisting of $NR^6C(O)$, $NR^6S(O)$, $NR^6S(O)_2$, NR^6S, NR^6O, SS, NR^6NR^6 and OC(O), with the remaining one of X, Y, and Z being CR^8R^9, or

(c) n is zero and X, Y and Z together constitute a moiety selected from the group consisting of



wherein wavy lines are bonds to the atoms of the depicted ring;

R^6 and $R^{6'}$ are independently selected from the group consisting of hydrido, C_1-C_6-alkanoyl, C_6-aryl-C_1-C_6-alkyl, aroyl, bis(C_1-C_6-alkoxy-C_1-C_6-alkyl)-C_1-C_6-alkyl, C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-perfluoroalkyl, C_1-C_6-trifluoromethylalkyl, C_1-C_6-perfluoroalkoxy-C_1-C_6-alkyl, C_1-C_6-alkoxy-C_1-C_6-alkyl, C_3-C_6-cycloalkyl, C_3-C_8-heterocycloalkyl, C_3-C_8-heterocycloalkylcarbonyl, C_6-aryl, C_5-C_6-heterocyclo, C_5-C_6-heteroaryl, C_3-C_8-cycloalkyl-C_1-C_6-alkyl, C_6-aryloxy-C_1-C_6-alkyl, heteroaryloxy-C_1-C_6-alkyl, heteroaryl-C_1-C_6-alkoxy-C_1-C_6-alkyl, heteroarylthio-C_1-C_6-alkyl, C_6-arylsulfonyl, C_1-C_6-alkylsulfonyl, C_5-C_6-heteroarylsulfonyl, carboxy-C_1-C_6-alkyl, C_1-C_4-alkoxycarbonyl-C_1-C_6-alkyl, aminocarbonyl, C_1-C_6-alkyliminocarbonyl, C_6-aryliminocarbonyl, C_5-C_6-heterocycloiminocarbonyl, C_6-arylthio-C_1-C_6-alkyl, C_1-C_6-alkylthio-C_1-C_6-alkyl, C_6-arylthio-C_3-C_6-alkenyl, C_1-C_4-alkylthio-C_3-C_6-alkenyl, C_5-C_6-heteroaryl-C_1-C_6-alkyl, halo-C_1-C_6-alkanoyl, hydroxy-C_1-C_6-alkanoyl, thiol-C_1-C_6-alkanoyl, C_3-C_6-alkenyl, C_3-C_6-alkynyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, C_1-C_5-alkoxycarbonyl, aryloxycarbonyl, NR^8R^9-C_1-C_5-alkylcarbonyl, hydroxy-C_1-C_5-alkyl, an aminocarbonyl wherein the aminocarbonyl nitrogen is (i) unsubstituted or (ii) substituted with one or two radicals independently selected from the group consisting of C_1-C_6-alkyl, ar-C_1-C_6-alkyl, C_3-C_8-cycloalkyl, and a C_1-C_6-alkanoyl group, hydroxyaminocarbonyl, an aminosulfonyl group wherein the aminosulfonyl nitrogen is (i) unsubstituted or (ii) substituted with one or two radicals independently selected from the group consisting of C_1-C_6-alkyl, ar-C_1-C_6-alkyl, C_3-C_8-cycloalkyl, and a C_1-C_6-alkanoyl group, an amino-C_1-C_6-alkylsulfonyl group wherein the amino-C_1-C_6-alkylsulfonyl nitrogen is (i) unsubstituted or (ii) substituted with one or two radicals independently selected from the group consisting of C_1-C_6-alkyl, ar-C_1-C_6-alkyl, C_3-C_8-cycloalkyl, and a C_1-C_6-alkanoyl group and an amino-C_1-C_6-alkyl group wherein the aminoalkyl nitrogen is (i) unsubstituted or (ii) substituted with one or two radicals independently selected from the

group consisting of C_1-C_6-alkyl, ar-C_1-C_6-alkyl, C_3-C_8-cycloalkyl, and a C_1-C_6-alkanoyl group;

R^7 is selected from the group consisting of a arylalkyl, aryl, heteroaryl, heterocyclo, C_1-C_6-alkyl, C_3-C_6-alkynyl, C_3-C_6-alkenyl, C_1-C_6-carboxyalkyl, and a C_1-C_6-hydroxyalkyl group];

as to R^8:

R^8 **is [and R^9 and R^{10} and R^{11} are independently]** selected from the group consisting of **[a]** hydrido, hydroxy, C_1-C_6-alkyl, C_1-C_6-alkanoyl, aroyl, aryl, ar-C_1-C_6-alkyl, heteroaryl, heteroar-C_1-C_6-alkyl, C_2-C_6-alkynyl, C_2-C_6-alkenyl, thiol-C_1-C_6-alkyl, C_1-C_6-alkylthio-C_1-C_6-alkyl, cycloalkyl, cycloalkyl-C_1-C_6-alkyl, **[heterocycloalkyl-C_1-C_6-alkyl] heterocyclo-C_1-C_6-alkyl**, C_1-C_6-alkoxy-C_1-C_6-alkyl, aralkoxy-C_1-C_6-alkyl, C_1-C_6-alkoxy-C_1-C_6-alkoxy-C_1-C_6-alkyl, hydroxy-C_1-C_6-alkyl, hydroxycarbonyl-C_1-C_6-alkyl, hydroxycarbonylar-C_1-C_6-alkyl, aminocarbonyl-C_1-C_6-alkyl, aryloxy-C_1-C_6-alkyl, heteroaryloxy-C_1-C_6-alkyl, arylthio-C_1-C_6-alkyl, heteroarylthio-C_1-C_6-alkyl, **a [the]** sulfoxide **[or sulfone]** of any of said thio substituents, **a sulfone of any said thio substituents,** perfluoro-C_1-C_6-alkyl, trifluoromethyl-C_1-C_6-alkyl, halo-C_1-C_6-alkyl, alkoxycarbonylamino-C_1-C_6-alkyl, and **[an]** amino-C_1-C_6-alkyl, **[group]** wherein:

the aminoalkyl nitrogen **optionally** is **[(i) unsubstituted or (ii)]** substituted with **up to [one or]** two **substituents [radicals]** independently selected from the group consisting of C_1-C_6-alkyl, ar-C_1-C_6-alkyl, cycloalkyl, and C_1-C_6-alkanoyl, **[or wherein]**

R^8 and R^9, **together with [or R^{10} and R^{11} and]** the carbon to which they are bonded, form a carbonyl group, or **[wherein]**

R^8 and R^9 or **[R^{10} and R^{11}, or]** R^8 and R^{10}, together with the **atom(s) [atoms]** to which they are bonded, form a 5- to 8-membered carbocyclic ring **[,]** or a 5- to 8-membered **[heterocyclic] heterocyclo** or heteroaryl ring **comprising [containing]** one or

two heteroatoms **independently selected from the group consisting of** **[that are]** nitrogen, oxygen, **and** **[or]** sulfur**;** **[, with the proviso that]**

as to R^9:

R^9 is selected from the group consisting of hydrido, hydroxy, C_1-C_6-alkyl, C_1-C_6-alkanoyl, aroyl, aryl, ar-C_1-C_6-alkyl, heteroaryl, heteroar-C_1-C_6-alkyl, C_2-C_6-alkynyl, C_2-C_6-alkenyl, thiol-C_1-C_6-alkyl, C_1-C_6-alkylthio-C_1-C_6-alkyl, cycloalkyl, cycloalkyl-C_1-C_6-alkyl, heterocyclo-C_1-C_6-alkyl, C_1-C_6-alkoxy-C_1-C_6-alkyl, aralkoxy-C_1-C_6-alkyl, C_1-C_6-alkoxy-C_1-C_6-alkoxy-C_1-C_6-alkyl, hydroxy-C_1-C_6-alkyl, hydroxycarbonyl-C_1-C_6-alkyl, hydroxycarbonylar-C_1-C_6-alkyl, aminocarbonyl-C_1-C_6-alkyl, aryloxy-C_1-C_6-alkyl, heteroaryloxy-C_1-C_6-alkyl, arylthio-C_1-C_6-alkyl, heteroarylthio-C_1-C_6-alkyl, a sulfoxide of any of said thio substituents, a sulfone of any said thio substituents, perfluoro-C_1-C_6-alkyl, trifluoromethyl-C_1-C_6-alkyl, halo-C_1-C_6-alkyl, alkoxycarbonylamino-C_1-C_6-alkyl, and amino-C_1-C_6-alkyl, wherein:

the aminoalkyl nitrogen optionally is substituted with up to two substituents independently selected from the group consisting of C_1-C_6-alkyl, ar-C_1-C_6-alkyl, cycloalkyl, and C_1-C_6-alkanoyl,

R^9 and R^8, together with the carbon to which they are bonded, form a carbonyl group, a 5- to 8-membered carbocyclic ring, or a 5- to 8-membered heterocyclo or heteroaryl ring comprising one or two heteroatoms independently selected from the group consisting of nitrogen, oxygen, and sulfur;

as to R^{10}:

R^{10} is selected from the group consisting of hydrido, hydroxy, C_1-C_6-alkyl, C_1-C_6-alkanoyl, aroyl, aryl, ar-C_1-C_6-alkyl, heteroaryl, heteroar-C_1-C_6-alkyl, C_2-C_6-alkynyl, C_2-C_6-alkenyl, thiol-C_1-C_6-alkyl, C_1-C_6-alkylthio-C_1-C_6-alkyl, cycloalkyl, cycloalkyl-C_1-C_6-alkyl, heterocyclo-C_1-C_6-alkyl, C_1-C_6-alkoxy-C_1-C_6-alkyl, aralkoxy-C_1-C_6-alkyl, C_1-C_6-alkoxy-C_1-C_6-alkoxy-C_1-C_6-alkyl, hydroxy-

C_1-C_6-alkyl, hydroxycarbonyl-C_1-C_6-alkyl, hydroxycarbonylar-C_1-C_6-alkyl, aminocarbonyl-C_1-C_6-alkyl, aryloxy-C_1-C_6-alkyl, heteroaryloxy-C_1-C_6-alkyl, arylthio-C_1-C_6-alkyl, heteroarylthio-C_1-C_6-alkyl, a sulfoxide of any of said thio substituents, a sulfone of any said thio substituents, perfluoro-C_1-C_6-alkyl, trifluoromethyl-C_1-C_6-alkyl, halo-C_1-C_6-alkyl, alkoxycarbonylamino-C_1-C_6-alkyl, and amino-C_1-C_6-alkyl, wherein:

the aminoalkyl nitrogen optionally is substituted with up to two substituents independently selected from the group consisting of C_1-C_6-alkyl, ar-C_1-C_6-alkyl, cycloalkyl, and C_1-C_6-alkanoyl,

R^{10} and R^{11}, together with the carbon to which they are bonded, form a carbonyl group, or

R^{10} and R^8 or R^{10} and R^{11}, together with the atom(s) to which they are bonded, form a 5- to 8-membered carbocyclic ring or a 5- to 8-membered heterocyclo or heteroaryl ring comprising one or two heteroatoms independently selected from the group consisting of nitrogen, oxygen, and sulfur;

as to R^{11}:

R^{11} is selected from the group consisting of hydrido, hydroxy, C_1-C_6-alkyl, C_1-C_6-alkanoyl, aroyl, aryl, ar-C_1-C_6-alkyl, heteroaryl, heteroar-C_1-C_6-alkyl, C_2-C_6-alkynyl, C_2-C_6-alkenyl, thiol-C_1-C_6-alkyl, C_1-C_6-alkylthio-C_1-C_6-alkyl, cycloalkyl, cycloalkyl-C_1-C_6-alkyl, heterocyclo-C_1-C_6-alkyl, C_1-C_6-alkoxy-C_1-C_6-alkyl, aralkoxy-C_1-C_6-alkyl, C_1-C_6-alkoxy-C_1-C_6-alkoxy-C_1-C_6-alkyl, hydroxy-C_1-C_6-alkyl, hydroxycarbonyl-C_1-C_6-alkyl, hydroxycarbonylar-C_1-C_6-alkyl, aminocarbonyl-C_1-C_6-alkyl, aryloxy-C_1-C_6-alkyl, heteroaryloxy-C_1-C_6-alkyl, arylthio-C_1-C_6-alkyl, heteroarylthio-C_1-C_6-alkyl, a sulfoxide of any of said thio substituents, a sulfone of any said thio substituents, perfluoro-C_1-C_6-alkyl, trifluoromethyl-C_1-C_6-alkyl, halo-C_1-C_6-alkyl, alkoxycarbonylamino-C_1-C_6-alkyl, and amino-C_1-C_6-alkyl, wherein:

the aminoalkyl nitrogen optionally is substituted with up to two substituents independently selected from the group consisting of C_1-C_6-alkyl, ar-C_1-C_6-alkyl, cycloalkyl, and C_1-C_6-alkanoyl,

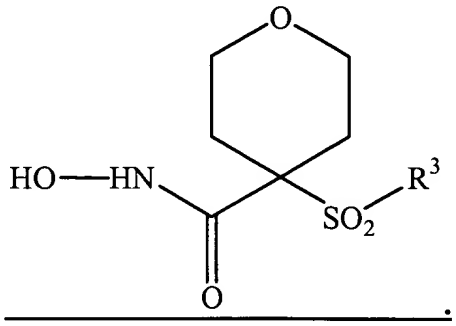
R^{11} and R^{10}, together with the carbon to which they are bonded, form a carbonyl group, a 5- to 8-membered carbocyclic ring, or a 5- to 8-membered heterocyclo or heteroaryl ring comprising one or two heteroatoms independently selected from the group consisting of nitrogen, oxygen, and sulfur; and

only one of R^8 and R^9 or R^{10} and R^{11} is hydroxy [;

R^{12} and $R^{12'}$ are independently selected from the group consisting of a hydrido, C_1-C_6-alkyl, aryl, ar-C_1-C_6-alkyl, heteroaryl, heteroaralkyl, C_2-C_6-alkynyl, C_2-C_6-alkenyl, thiol-C_1-C_6-alkyl, cycloalkyl, cycloalkyl-C_1-C_6-alkyl, heterocycloalkyl-C_1-C_6-alkyl, C_1-C_6-alkoxy-C_1-C_6-alkyl, aryloxy-C_1-C_6-alkyl, amino-C_1-C_6-alkyl, C_1-C_6-alkoxy-C_1-C_6-alkoxy-C_1-C_6-alkyl, hydroxy-C_1-C_6-alkyl, hydroxycarbonyl-C_1-C_6-alkyl, hydroxycarbonylar-C_1-C_6-alkyl, aminocarbonyl-C_1-C_6-alkyl, aryloxy-C_1-C_6-alkyl, heteroaryloxy-C_1-C_6-alkyl, C_1-C_6-alkylthio-C_1-C_6-alkyl, arylthio-C_1-C_6-alkyl, heteroarylthio-C_1-C_6-alkyl, the sulfoxide or sulfone of any said thio substituents, perfluoro-C_1-C_6-alkyl, trifluoromethyl-C_1-C_6-alkyl, halo-C_1-C_6-alkyl, alkoxycarbonylamino-C_1-C_6-alkyl, and an amino-C_1-C_6-alkyl group wherein the aminoalkyl nitrogen is (i) unsubstituted or (ii) substituted with one or two radicals independently selected from the group consisting of C_1-C_6-alkyl, ar-C_1-C_6-alkyl, cycloalkyl and C_1-C_6-alkanoyl; and

R^{13} is selected from the group consisting of a hydrido, benzyl, phenyl, C_1-C_6-alkyl, C_2-C_6-alkynyl, C_2-C_6-alkenyl and a C_1-C_6-hydroxyalkyl group].

16. **(amended once)** The process according to claim 15, wherein the **[sum of m + n + p = 1 or 2]** **compound corresponds in structure to the following formula:**

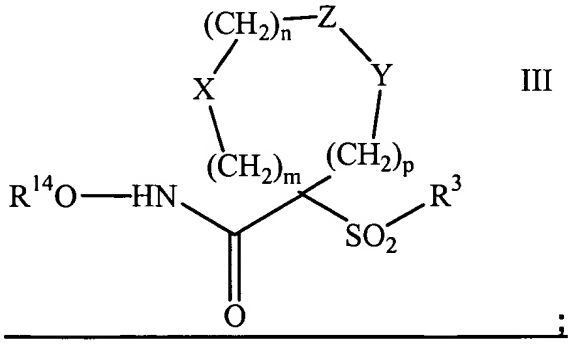


Claims 17-19 have been canceled without prejudice to their patentability.

20. **(amended once)** A process for treating a host mammal having **[a condition associated with pathological matrix metalloprotease (MMP) activity]** **angiogenesis, wherein:**

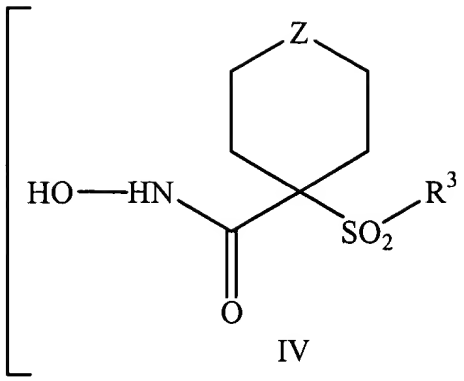
the process **[that]** comprises administering a **[metalloprotease inhibitor]** compound or a pharmaceutically acceptable salt thereof in an effective amount to a mammalian host having **angiogenesis, the compound or salt** **[such a condition, said metalloprotease inhibitor]** inhibiting the activity of one or more of MMP-2, MMP-9, and MMP-13, while exhibiting substantially less inhibitory activity against MMP-1; **[, said]**

the compound **corresponds** **[corresponding]** in structure to formula **III:** **[IV, below]**



III

;



IV

wherein]

R^{14} is hydrido, a pharmaceutically acceptable cation, or $C(W)R^{15}$;

W is O or S;

R^{15} is selected from the group consisting of C_1-C_6-alkyl, aryl, C_1-C_6-alkoxy, heteroaryl-C_1-C_6-alkyl, C_3-C_8-cycloalkyl-C_1-C_6-alkyl, aryloxy, ar-C_1-C_6-alkoxy, ar-C_1-C_6-alkyl, heteroaryl, and amino-C_1-C_6-alkyl, wherein the amino-C_1-C_6-alkyl nitrogen optionally is substituted with:

up to two substituents independently selected from the group consisting of C_1-C_6-alkyl, aryl, ar-C_1-C_6-alkyl, C_3-C_8-cycloalkyl-C_1-C_6-alkyl, ar-C_1-C_6-alkoxycarbonyl, C_1-C_6-alkoxycarbonyl, and C_1-C_6-alkanoyl, or

two substituents such that the two substituents, together with the amino-C_1-C_6-alkyl nitrogen, form a 5- to 8-membered heterocyclo or heteroaryl ring;

m is zero, 1, or 2;

n is zero, 1, or 2;

p is zero, 1, or 2;

the sum of m + n + p is 2;

one of X, Y, and Z is O, and the remaining two of X, Y, and Z are CR^8R^9 and $CR^{10}R^{11}$;

as to R^8:

R^8 is selected from the group consisting of hydrido, hydroxy, C_1-C_6-alkyl, C_1-C_6-alkanoyl, aroyl, aryl, ar-C_1-C_6-alkyl, heteroaryl, heteroar-C_1-C_6-alkyl, C_2-C_6-alkynyl, C_2-C_6-alkenyl, thiol-C_1-C_6-alkyl, C_1-C_6-alkylthio-C_1-C_6-alkyl, cycloalkyl, cycloalkyl-C_1-C_6-alkyl, heterocyclo-C_1-C_6-alkyl, C_1-C_6-alkoxy-C_1-C_6-alkyl, aralkoxy-C_1-C_6-alkyl, C_1-C_6-alkoxy-C_1-C_6-alkoxy-C_1-C_6-alkyl, hydroxy-C_1-C_6-alkyl, hydroxycarbonyl-C_1-C_6-alkyl, hydroxycarbonylar-C_1-C_6-alkyl, aminocarbonyl-C_1-C_6-alkyl, aryloxy-C_1-C_6-alkyl, heteroaryloxy-C_1-C_6-alkyl, arylthio-C_1-C_6-alkyl, heteroarylthio-C_1-C_6-alkyl, a sulfoxide of any of said thio substituents, a sulfone of any said thio substituents, perfluoro-C_1-C_6-alkyl, trifluoromethyl-C_1-C_6-alkyl, halo-C_1-C_6-alkyl, alkoxycarbonylamino-C_1-C_6-alkyl, and amino-C_1-C_6-alkyl, wherein:

the aminoalkyl nitrogen optionally is substituted with up to two substituents independently selected from the group consisting of C_1-C_6-alkyl, ar-C_1-C_6-alkyl, cycloalkyl, and C_1-C_6-alkanoyl,

R^8 and R^9, together with the carbon to which they are bonded, form a carbonyl group, or

R^8 and R^9 or R^8 and R^{10}, together with the atom(s) to which they are bonded, form a 5- to 8-membered carbocyclic ring or a 5- to 8-membered heterocyclo or heteroaryl ring comprising one or two heteroatoms independently selected from the group consisting of nitrogen, oxygen, and sulfur;

as to R^9:

R^9 is selected from the group consisting of hydrido, hydroxy, C_1-C_6-alkyl, C_1-C_6-alkanoyl, aroyl, aryl, ar-C_1-C_6-alkyl, heteroaryl, heteroar-C_1-C_6-alkyl, C_2-C_6-alkynyl, C_2-C_6-alkenyl, thiol-C_1-C_6-alkyl, C_1-C_6-alkylthio-C_1-C_6-alkyl, cycloalkyl, cycloalkyl-C_1-C_6-alkyl, heterocyclo-C_1-C_6-alkyl, C_1-C_6-alkoxy-C_1-C_6-alkyl, aralkoxy-C_1-C_6-alkyl, C_1-C_6-alkoxy-C_1-C_6-alkoxy-C_1-C_6-alkyl, hydroxy-

C_1-C_6-alkyl, hydroxycarbonyl-C_1-C_6-alkyl, hydroxycarbonylar-C_1-C_6-alkyl, aminocarbonyl-C_1-C_6-alkyl, aryloxy-C_1-C_6-alkyl, heteroaryloxy-C_1-C_6-alkyl, arylthio-C_1-C_6-alkyl, heteroarylthio-C_1-C_6-alkyl, a sulfoxide of any of said thio substituents, a sulfone of any said thio substituents, perfluoro-C_1-C_6-alkyl, trifluoromethyl-C_1-C_6-alkyl, halo-C_1-C_6-alkyl, alkoxycarbonylamino-C_1-C_6-alkyl, and amino-C_1-C_6-alkyl, wherein:

the aminoalkyl nitrogen optionally is substituted with up to two substituents independently selected from the group consisting of C_1-C_6-alkyl, ar-C_1-C_6-alkyl, cycloalkyl, and C_1-C_6-alkanoyl,

R^9 and R^8, together with the carbon to which they are bonded, form a carbonyl group, a 5- to 8-membered carbocyclic ring, or a 5- to 8-membered heterocyclo or heteroaryl ring comprising one or two heteroatoms independently selected from the group consisting of nitrogen, oxygen, and sulfur;

as to R^{10}:

R^{10} is selected from the group consisting of hydrido, hydroxy, C_1-C_6-alkyl, C_1-C_6-alkanoyl, aroyl, aryl, ar-C_1-C_6-alkyl, heteroaryl, heteroar-C_1-C_6-alkyl, C_2-C_6-alkynyl, C_2-C_6-alkenyl, thiol-C_1-C_6-alkyl, C_1-C_6-alkylthio-C_1-C_6-alkyl, cycloalkyl, cycloalkyl-C_1-C_6-alkyl, heterocyclo-C_1-C_6-alkyl, C_1-C_6-alkoxy-C_1-C_6-alkyl, aralkoxy-C_1-C_6-alkyl, C_1-C_6-alkoxy-C_1-C_6-alkoxy-C_1-C_6-alkyl, hydroxy-C_1-C_6-alkyl, hydroxycarbonyl-C_1-C_6-alkyl, hydroxycarbonylar-C_1-C_6-alkyl, aminocarbonyl-C_1-C_6-alkyl, aryloxy-C_1-C_6-alkyl, heteroaryloxy-C_1-C_6-alkyl, arylthio-C_1-C_6-alkyl, heteroarylthio-C_1-C_6-alkyl, a sulfoxide of any of said thio substituents, a sulfone of any said thio substituents, perfluoro-C_1-C_6-alkyl, trifluoromethyl-C_1-C_6-alkyl, halo-C_1-C_6-alkyl, alkoxycarbonylamino-C_1-C_6-alkyl, and amino-C_1-C_6-alkyl, wherein:

the aminoalkyl nitrogen optionally is substituted with up to two substituents independently selected from the group consisting of C_1-C_6-alkyl, ar-C_1-C_6-alkyl, cycloalkyl, and C_1-C_6-alkanoyl,

R^{10} and R^{11}, together with the carbon to which they are bonded, form a carbonyl group, or

R^{10} and R^8 or R^{10} and R^{11}, together with the atom(s) to which they are bonded, form a 5- to 8-membered carbocyclic ring or a 5- to 8-membered heterocyclo or heteroaryl ring comprising one or two heteroatoms independently selected from the group consisting of nitrogen, oxygen, and sulfur;

as to R^{11}:

R^{11} is selected from the group consisting of hydrido, hydroxy, C_1-C_6-alkyl, C_1-C_6-alkanoyl, aroyl, aryl, ar-C_1-C_6-alkyl, heteroaryl, heteroar-C_1-C_6-alkyl, C_2-C_6-alkynyl, C_2-C_6-alkenyl, thiol-C_1-C_6-alkyl, C_1-C_6-alkylthio-C_1-C_6-alkyl, cycloalkyl, cycloalkyl-C_1-C_6-alkyl, heterocyclo-C_1-C_6-alkyl, C_1-C_6-alkoxy-C_1-C_6-alkyl, aralkoxy-C_1-C_6-alkyl, C_1-C_6-alkoxy-C_1-C_6-alkoxy-C_1-C_6-alkyl, hydroxy-C_1-C_6-alkyl, hydroxycarbonyl-C_1-C_6-alkyl, hydroxycarbonylar-C_1-C_6-alkyl, aminocarbonyl-C_1-C_6-alkyl, aryloxy-C_1-C_6-alkyl, heteroaryloxy-C_1-C_6-alkyl, arylthio-C_1-C_6-alkyl, heteroarylthio-C_1-C_6-alkyl, a sulfoxide of any of said thio substituents, a sulfone of any said thio substituents, perfluoro-C_1-C_6-alkyl, trifluoromethyl-C_1-C_6-alkyl, halo-C_1-C_6-alkyl, alkoxycarbonylamino-C_1-C_6-alkyl, and amino-C_1-C_6-alkyl, wherein:

the aminoalkyl nitrogen optionally is substituted with up to two substituents independently selected from the group consisting of C_1-C_6-alkyl, ar-C_1-C_6-alkyl, cycloalkyl, and C_1-C_6-alkanoyl,

R^{11} and R^{10}, together with the carbon to which they are bonded, form a carbonyl group, a 5- to 8-membered carbocyclic ring, or a 5- to 8-membered

heterocyclo or heteroaryl ring comprising one or two heteroatoms independently selected from the group consisting of nitrogen, oxygen, and sulfur;

only one of R^8 and R^9 or R^{10} and R^{11} is hydroxy; and

R^3 is **[an optionally]** substituted aryl or **[optionally]** substituted heteroaryl **[radical, and when said aryl or heteroaryl radical is substituted]**, wherein:

the substituent **on the aryl or heteroaryl** is **[(a)]** selected from the group consisting of **[an]** optionally substituted cycloalkyl, **[heterocycloalkyl] heterocyclo**, aryl, heteroaryl, aralkyl, heteroaralkyl, aralkoxy, heteroaralkoxy, aralkoxyalkyl, aryloxyalkyl, aralkanoylalkyl, arylcarbonylalkyl, aralkylaryl, aryloxyalkylaryl, aralkoxyaryl, arylazoaryl, arylhydrazinoaryl, alkylthioaryl, arylthioalkyl, alkylthioaralkyl, aralkylthioalkyl, **[an]** aralkylthioaryl**, a [radical, the]** sulfoxide **[or sulfone]** of any of the thio substituents, **a sulfone of any of the thio substituents,** and a fused ring structure comprising **at least** two **[or more]** 5- **to [or]** 6-membered rings **independently** selected from the group consisting of aryl, heteroaryl, cycloalkyl**,** and **[heterocycloalkyl] heterocyclo, wherein: [and (b)]**

each optional substituent of any such group is **[itself optionally substituted with one or more substituents]** independently selected from the group consisting of **[a]** cyano, perfluoroalkyl, trifluoromethoxy, trifluoromethylthio, haloalkyl, trifluoromethylalkyl, aralkoxycarbonyl, aryloxycarbonyl, hydroxy, halo, alkyl, alkoxy, nitro, thiol, hydroxycarbonyl, aryloxy, arylthio, aralkyl, aryl, arylcarbonylamino, heteroaryloxy, heteroarylthio, heteroaralkyl, cycloalkyl, heterocyclooxy, heterocyclothio, heterocycloamino, cycloalkyloxy, cycloalkylthio, heteroaralkoxy, heteroaralkylthio, aralkoxy, aralkylthio, aralkylamino, heterocyclo, heteroaryl, arylazo, hydroxycarbonylalkoxy, alkoxycarbonylalkoxy, alkanoyl, arylcarbonyl, aralkanoyl, alkanoyloxy, aralkanoyloxy, hydroxyalkyl, hydroxyalkoxy, alkylthio, alkoxyalkylthio, alkoxycarbonyl, aryloxyalkoxyaryl, arylthioalkylthioaryl, aryloxyalkylthioaryl, arylthioalkoxyaryl, hydroxycarbonylalkoxy, hydroxycarbonylalkylthio, alkoxycarbonylalkoxy, alkoxycarbonylalkylthio, amino, **carbonylamino, and aminoalkyl,** wherein:

the amino nitrogen **optionally** is **[(i) unsubstituted, or (ii)]** substituted with**:**

up to [one or] two substituents **[that are]** independently selected from the group consisting of **[an]** alkyl, aryl, heteroaryl, aralkyl, cycloalkyl, aralkoxycarbonyl, alkoxycarbonyl, arylcarbonyl, aralkanoyl, heteroarylcarbonyl, heteroaralkanoyl**,** and **[an]** alkanoyl **[group]**, or **[(iii) wherein the amino nitrogen and]**

two substituents **such that the two substituents, together with the amino nitrogen, [attached thereto]** form a 5- to 8-membered heterocyclo or heteroaryl ring **that optionally: [containing zero]**

comprises up to two additional heteroatoms **independently selected from the group consisting of [that are]** nitrogen, oxygen **and [or]** sulfur**,** and **[which ring itself]**

is **[(a) unsubstituted or (b)]** substituted with **up to [one or]** two **substituents [groups]** independently selected from the group consisting of **[an]** aryl, alkyl, heteroaryl, aralkyl, heteroaralkyl, hydroxy, alkoxy, alkanoyl, cycloalkyl, **[heterocycloalkyl] heterocyclo**, alkoxycarbonyl, hydroxyalkyl, trifluoromethyl, benzofused **[heterocycloalkyl] heterocyclo**, hydroxyalkoxyalkyl, aralkoxycarbonyl, hydroxycarbonyl, aryloxycarbonyl, benzofused heterocycloalkoxy, benzofused cycloalkylcarbonyl, heterocyclo-alkylcarbonyl, and **[a]** cycloalkylcarbonyl**, [group, carbonylamino wherein]**, the carbonylamino nitrogen **optionally** is**: [(i) unsubstituted, or (ii) is]**

the reacted amine of an amino acid, **[or (iii)]**

substituted with **up to [one or]** two **substituents independently [radicals]** selected from the group consisting of

[an] alkyl, hydroxyalkyl, hydroxyheteroaralkyl, cycloalkyl, aralkyl, trifluoromethylalkyl, **[heterocycloalkyl]** **heterocyclo**, benzofused **[heterocycloalkyl]** **heterocyclo**, **[benzofused heterocycloalkyl,]** benzofused cycloalkyl, and **[an]** N,N-dialkylsubstituted alkylamino-alkyl **[group]**, or **[(iv) the carboxamido nitrogen and]**

substituted with two substituents **such that the two substituents, [bonded thereto]** together **with the carbonylamino nitrogen,** form a 5- to 8-membered heterocyclo, heteroaryl, or benzofused **[heterocycloalkyl]** **heterocyclo, wherein: [ring that]**

the heterocyclo, heteroaryl, or benzofused heterocyclo optionally is **[itself unsubstituted or]** substituted with **up to [one or]** two **substituents [radicals]** independently selected from the group consisting of **[an]** alkyl, alkoxycarbonyl, nitro, **[heterocycloalkyl]** **heterocyclo**, hydroxy, hydroxycarbonyl, aryl, aralkyl, heteroaralkyl, and **[an]** amino **[group]**, wherein the amino nitrogen **optionally** is **[(i) unsubstituted, or (ii)]** substituted with:

up to [one or] two substituents **[that are]** independently selected from the group consisting of alkyl, aryl, and heteroaryl, or **[(iii) wherein the amino nitrogen and]**

two substituents **such that the two substituents, together with the amino nitrogen, [attached thereto]** form a 5- to 8-membered heterocyclo or heteroaryl ring; **[, and an aminoalkyl group wherein]**

the aminoalkyl nitrogen **optionally** is **[(i) unsubstituted, or (ii)]** substituted with:

up to [one or] two substituents independently selected from the group consisting of **[an]** alkyl, aryl, aralkyl, cycloalkyl, aralkoxycarbonyl, alkoxycarbonyl, and **[an]** alkanoyl **[group]**, or **[(iii) wherein the aminoalkyl nitrogen and]**

two substituents **such that the two substituents, together with the aminoalkyl nitrogen, [attached thereto]** form a 5- to 8 membered heterocyclo or heteroaryl ring **[;**

Z is selected group the group consisting of O, S, NR^6, SO, SO_2, and NSO_2R^7,

wherein R^6 is selected from the group consisting of hydrido, C_1-C_5-alkyl, C_1-C_5-alkanoyl, benzyl, benzoyl, C_3-C_5-alkynyl, C_3-C_5-alkenyl, C_1-C_3-alkoxy-C_1-C_4-alkyl, C_3-C_6-cycloalkyl, heteroaryl-C_1-C_6-alkyl, C_1-C_5-hydroxyalkyl, C_1-C_5-carboxyalkyl, C_1-C_5-alkoxy C_1-C_5-alkylcarbonyl, and NR^8R^9-C_1-C_5-alkylcarbonyl or NR^8R^9-C_1-C_5-alkyl wherein R^8 and R^9 are independently hydrido, C_1-C_5-alkyl, C_1-C_5-alkoxycarbonyl or aryl-C_1-C_5-alkoxycarbonyl, or NR^8R^9 together form a heterocyclic ring containing 5- to 8-atoms in the ring; and

R^7 is selected from the group consisting of a arylalkyl, aryl, heteroaryl, heterocyclo, C_1-C_6-alkyl, C_3-C_6-alkynyl, C_3-C_6-alkenyl, C_1-C_6-carboxyalkyl and a C_1-C_6-hydroxyalkyl group].

21. **(amended once)** The process according to claim 20, wherein R^3 is a **5- or 6-membered [single-ringed]** aryl or **5- or 6-membered** heteroaryl group **[that is 5- or 6-membered]**, **wherein:**

the aryl or heteroaryl [and] is **[itself]** substituted at its own 4-position when a 6-membered ring or at its own 3- or 4-position when a 5-membered ring with a substituent selected from the group consisting of **[one other]** single-ringed aryl, **single-ringed [or]** heteroaryl, **[group, a]** N-piperidyl, **[group, a]** N-piperazinyl, **[group, a]** phenoxy, **[group, a]** thiophenoxy, **[group, a]** 4-thiopyridyl, **[group, a]** phenylazo, **[group]** and **[a]** benzamido **[group]**.

22. **(amended once)** The process according to claim 20, wherein R^3 has a length that is greater than that of a pentyl group and **[a length that is]** less than that of an icosyl group.

Claims 23-25 have been canceled without prejudice to their patentability.

26. **(amended once)** The process according to claim **20, [25]** wherein **R^3 comprises [said -G-A-R-E-Y substituent contains]** two to four **ring structures independently selected from the group consisting of cycloalkyl, aryl, heterocyclo, and heteroaryl [carbocyclic or heterocyclic rings]**.

27. **(amended once)** The process according to claim 26, wherein each of the two to four **ring structures [rings]** is 6-membered.

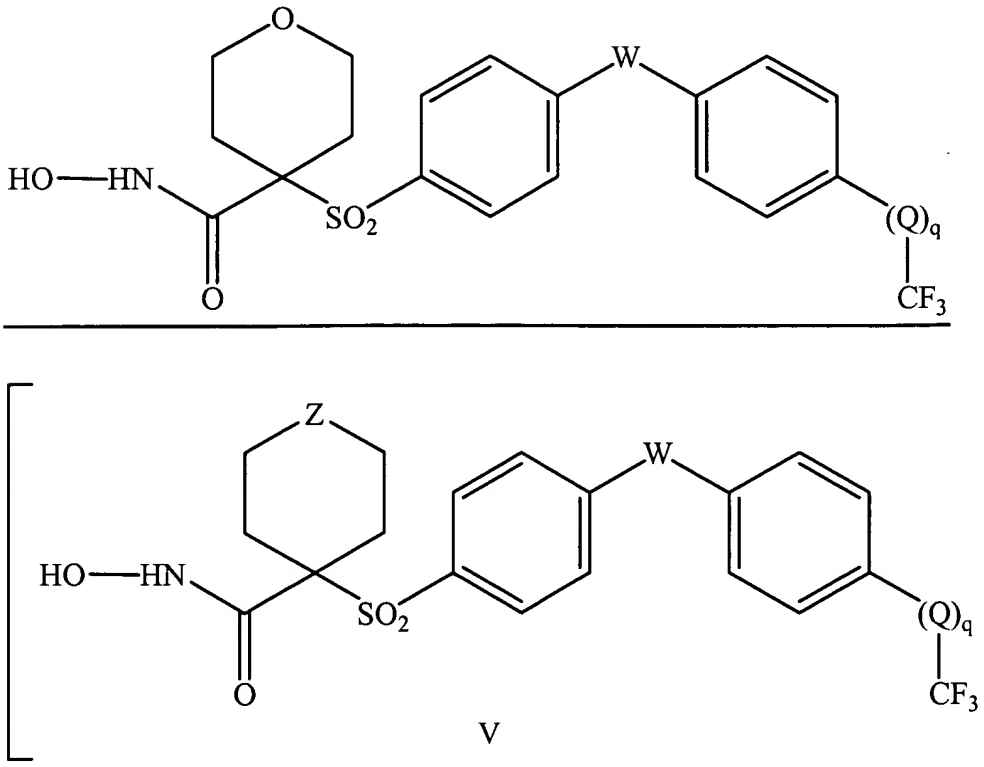
28. **(amended once)** The process according to claim **20, [25]** wherein **R^3 [said -G-A-R-E-Y substituent]** has a length that is greater than **that of** an octyl group and **[a length that is]** less than that of a stearyl group.

Claims 29-33 have been canceled without prejudice to their patentability.

35. **(amended once)** A process for treating a host mammal having **[a condition associated with pathological matrix metalloprotease (MMP) activity] angiogenesis, wherein:**

the process [that] comprises administering a **[metalloprotease inhibitor]** compound or a pharmaceutically acceptable salt thereof in an effective amount to a mammalian host having **angiogenesis, the compound or salt [such a condition, said metalloprotease inhibitor]** inhibiting the activity of one or more of MMP-2, MMP-9, and MMP-13, while exhibiting substantially less inhibitory activity against MMP-1; **[, said]**

the compound **corresponds** **[corresponding]** in structure to **the** formula **[V,]** below**:**



V

wherein

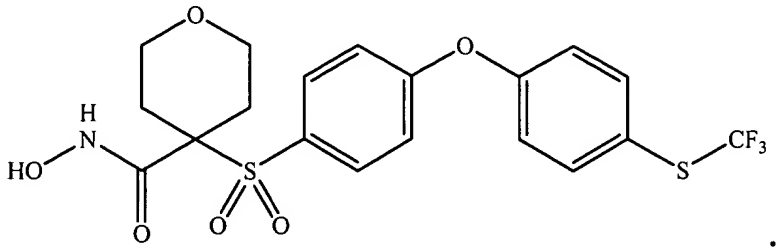
Z is O, S or NR^6];

W and Q are independently oxygen (O), NR^6, or sulfur (S)**;** **[,]**

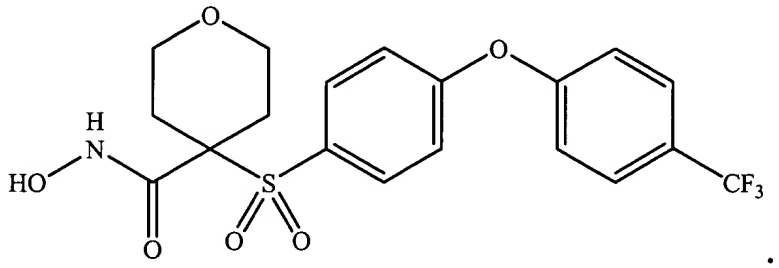
R^6 is selected from the group consisting of C_3-C_6-cycloalkyl, C_1-C_6-alkyl, C_3-C_6-alkenyl, C_3-C_6-alkynyl, C_1-C_6-alkoxy-C_1-C_6-alkyl, amino-C_1-C_6-alkyl, aminosulfonyl, heteroaryl-C_1-C_6-alkyl, aryloxycarbonyl, and C_1-C_6-alkoxycarbonyl; and

q is zero or one such that when q is zero, Q is absent and the trifluoromethyl group is bonded directly to the depicted phenyl ring.

41. **(amended once)** The process according to claim 35, wherein **the compound** **[said inhibitor]** corresponds in structure to the **following** formula:

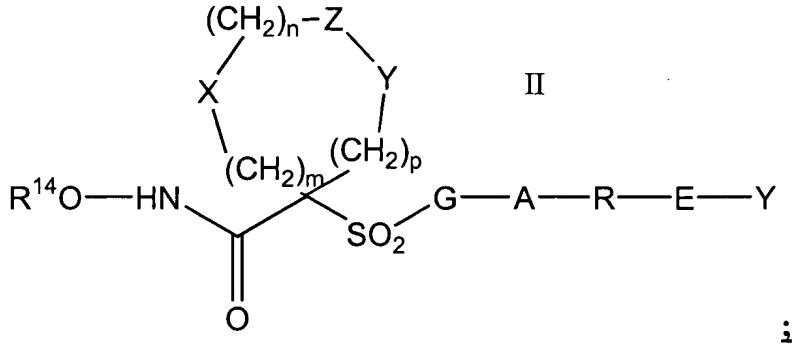


42. **(amended once)** The process according to claim 35, wherein **the compound** **[said inhibitor]** corresponds in structure to the **following** formula:



52. **(amended once)** A compound **or a salt thereof, wherein:**

the compound corresponds **[corresponding]** in structure to formula II **[, below, or a pharmaceutically acceptable salt thereof]**:



II

[wherein]

R^{14} is hydrido, a pharmaceutically acceptable cation, or $C(W)R^{15}$; **[where]**

W is O or S; **[and]**

R^{15} is selected from the group consisting of **[a]** C_1-C_6-alkyl, aryl, C_1-C_6-alkoxy, heteroaryl-C_1-C_6-alkyl, C_3-C_8-cycloalkyl-C_1-C_6-alkyl, aryloxy, ar-C_1-C_6-alkoxy, ar-C_1-C_6-

alkyl, heteroaryl, and amino-C_1-C_6-alkyl, **[group]** wherein the aminoalkyl nitrogen **optionally** is **[(i) unsubstituted or (ii)]** substituted with:

up to [one or] two substituents independently selected from the group consisting of **[an]** C_1-C_6-alkyl, aryl, ar-C_1-C_6-alkyl, C_3-C_8-cycloalkyl-C_1-C_6-alkyl, ar-C_1-C_6-alkoxycarbonyl, C_1-C_6-alkoxycarbonyl, and C_1-C_6-alkanoyl **[radical]**, or **[(iii) wherein the amino C_1-C_6-alkyl nitrogen and]**

two substituents **such that the two substituents, together with the amino-C_1-C_6-alkyl nitrogen, [attached thereto]** form a 5- to 8-membered heterocyclo or heteroaryl ring;

m is zero, 1, or 2;

n is zero, 1, or 2;

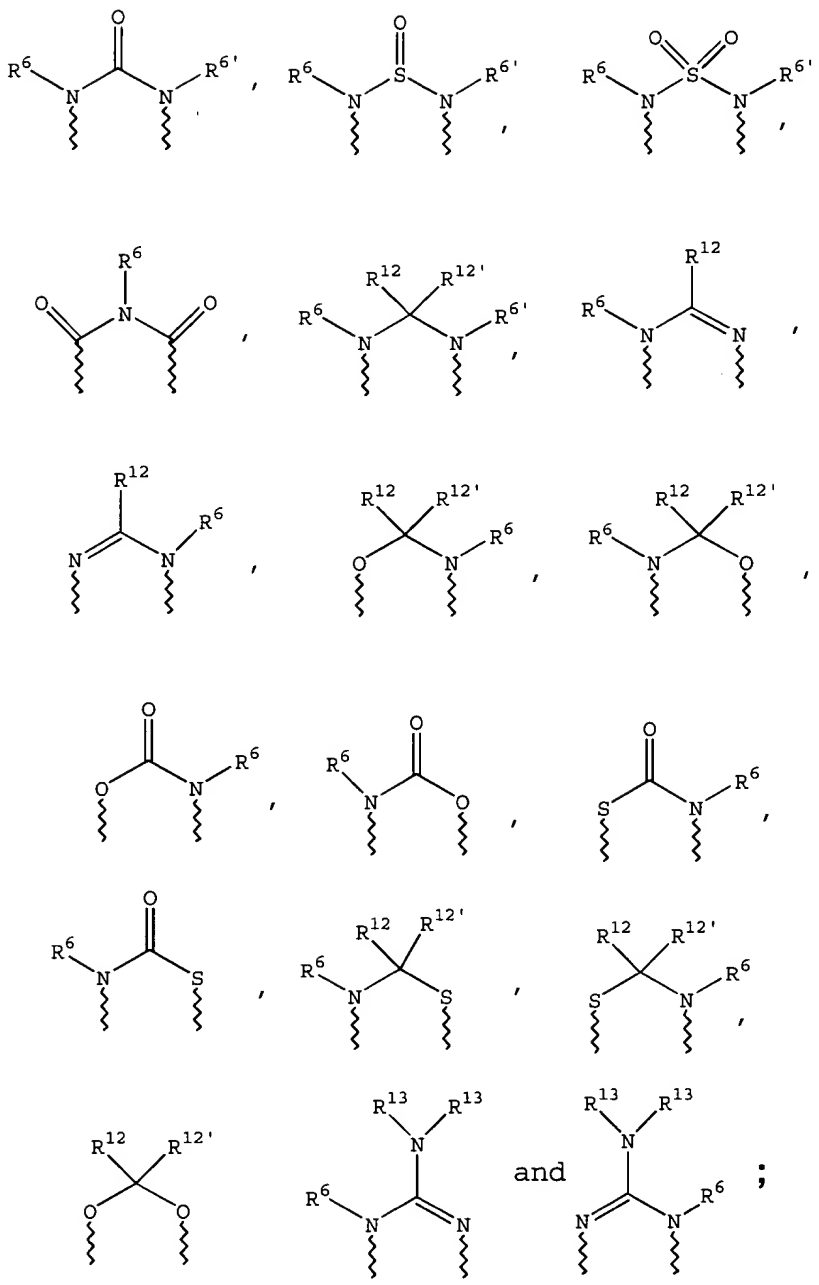
p is zero, 1, or 2;

the sum of m + n + p = **[1,]** 2 **[, 3 or 4]**;

[(a)] one of X, Y, and Z is **[selected from the group consisting of C(O), NR^6,]** O, **[S, S(O), $S(O)_2$ and $NS(O)_2R^7$,]** and the remaining two of X, Y, and Z are CR^8R^9 **[,]** and $CR^{10}R^{11}$ **[, or**

(b) X and Z or Z and Y together constitute a moiety that is selected from the group consisting of $NR^6C(O)$, $NR^6S(O)$, $NR^6S(O)_2$, NR^6S, NR^6O, SS, NR^6NR^6, and OC(O), with the remaining one of X, Y and Z being CR^8R^9, or

(c) n is zero and X, Y and Z together constitute a moiety selected from the group consisting of



wherein wavy lines are bonds to the atoms of the depicted ring;

R^6 and $R^{6'}$ are independently selected from the group consisting of hydrido, C_1-C_6-alkanoyl, C_6-aryl-C_1-C_6-alkyl, aroyl, bis(C_1-C_6-alkoxy-C_1-C_6-alkyl)-C_1-C_6-alkyl, C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-perfluoroalkyl, C_1-C_6-trifluoromethylalkyl, C_1-C_6-perfluoroalkoxy-C_1-C_6-alkyl, C_1-C_6-alkoxy-C_1-C_6-alkyl, C_3-C_6-cycloalkyl, C_3-C_8-

heterocycloalkyl, C_3-C_8-heterocycloalkylcarbonyl, C_6-aryl, C_5-C_6-heterocyclo, C_5-C_6-heteroaryl, C_3-C_8-cycloalkyl-C_1-C_6-alkyl, C_6-aryloxy-C_1-C_6-alkyl, heteroaryloxy-C_1-C_6-alkyl, heteroaryl-C_1-C_6-alkoxy-C_1-C_6-alkyl, heteroarylthio-C_1-C_6-alkyl, C_6-arylsulfonyl, C_1-C_6-alkylsulfonyl, C_5-C_6-heteroarylsulfonyl, carboxy-C_1-C_6-alkyl, C_1-C_4-alkoxycarbonyl-C_1-C_6-alkyl, aminocarbonyl, C_1-C_6-alkyliminocarbonyl, C_6-aryliminocarbonyl, C_5-C_6-heterocycloiminocarbonyl, C_6-arylthio-C_1-C_6-alkyl, C_1-C_6-alkylthio-C_1-C_6-alkyl, C_6-arylthio-C_3-C_6-alkenyl, C_1-C_4-alkylthio-C_3-C_6-alkenyl, C_5-C_6-heteroaryl-C_1-C_6-alkyl, halo-C_1-C_6-alkanoyl, hydroxy-C_1-C_6-alkanoyl, thiol-C_1-C_6-alkanoyl, C_3-C_6-alkenyl, C_3-C_6-alkynyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, C_1-C_5-alkoxycarbonyl, aryloxycarbonyl, NR^8R^9-C_1-C_5-alkylcarbonyl, hydroxy-C_1-C_5-alkyl, an aminocarbonyl wherein the aminocarbonyl nitrogen is (i) unsubstituted or (ii) substituted with one or two radicals independently selected from the group consisting of C_1-C_6-alkyl, ar-C_1-C_6-alkyl, C_3-C_8-cycloalkyl and a C_1-C_6-alkanoyl group, hydroxyaminocarbonyl, an aminosulfonyl group wherein the aminosulfonyl nitrogen is (i) unsubstituted or (ii) substituted with one or two radicals independently selected from the group consisting of C_1-C_6-alkyl, ar-C_1-C_6-alkyl, C_3-C_8-cycloalkyl and a C_1-C_6-alkanoyl group, an amino-C_1-C_6-alkylsulfonyl group wherein the amino-C_1-C_6-alkylsulfonyl nitrogen is (i) unsubstituted or (ii) substituted with one or two radicals independently selected from the group consisting of C_1-C_6-alkyl, ar-C_1-C_6-alkyl, C_3-C_8-cycloalkyl and a C_1-C_6-alkanoyl group and an amino-C_1-C_6-alkyl group, wherein the aminoalkyl nitrogen is (i) unsubstituted or (ii) substituted with one or two radicals independently selected from the group consisting of C_1-C_6-alkyl, ar-C_1-C_6-alkyl, C_3-C_8-cycloalkyl and a C_1-C_6-alkanoyl group;

R^7 is selected from the group consisting of a arylalkyl, aryl, heteroaryl, heterocyclo, C_1-C_6-alkyl, C_3-C_6-alkynyl, C_3-C_6-alkenyl, C_1-C_6-carboxyalkyl and a C_1-C_6-hydroxyalkyl group];

<u>as to R^8:</u>

R^8 **is** **[and R^9 and R^{10} and R^{11} are independently]** selected from the group consisting of **[a]** hydrido, hydroxy, C_1-C_6-alkyl, C_1-C_6-alkanoyl, aroyl, aryl, ar-C_1-C_6-alkyl, heteroaryl, heteroar-C_1-C_6-alkyl, C_2-C_6-alkynyl, C_2-C_6-alkenyl, thiol-C_1-C_6-alkyl, C_1-C_6-alkylthio-C_1-C_6-alkyl, cycloalkyl, cycloalkyl-C_1-C_6-alkyl, **[heterocycloalkyl-C_1-C_6-alkyl]** **heterocyclo-C_1-C_6-alkyl**, C_1-C_6-alkoxy-C_1-C_6-alkyl, aralkoxy-C_1-C_6-alkyl, C_1-C_6-alkoxy-C_1-C_6-alkoxy-C_1-C_6-alkyl, hydroxy-C_1-C_6-alkyl, hydroxycarbonyl-C_1-C_6-alkyl, hydroxycarbonylar-C_1-C_6-alkyl, aminocarbonyl-C_1-C_6-alkyl, aryloxy-C_1-C_6-alkyl, heteroaryloxy-C_1-C_6-alkyl, arylthio-C_1-C_6-alkyl, heteroarylthio-C_1-C_6-alkyl, **a** **[the]** sulfoxide **[or sulfone]** of any of said thio substituents, **a sulfone of any said thio substituents,** perfluoro-C_1-C_6-alkyl, trifluoromethyl-C_1-C_6-alkyl, halo-C_1-C_6-alkyl, alkoxycarbonylamino-C_1-C_6-alkyl, and **[an]** amino-C_1-C_6-alkyl, **[group]** wherein:

the aminoalkyl nitrogen **optionally** is **[(i) unsubstituted or (ii)]** substituted with **up to** **[one or]** two **substituents** **[radicals]** independently selected from the group consisting of C_1-C_6-alkyl, ar-C_1-C_6-alkyl, cycloalkyl, and C_1-C_6-alkanoyl, **[or wherein]**

R^8 and R^9, **together with** **[or R^{10} and R^{11} and]** the carbon to which they are bonded, form a carbonyl group, or **[wherein]**

R^8 and R^9 or **[R^{10} and R^{11}, or]** R^8 and R^{10}, together with the **atom(s)** **[atoms]** to which they are bonded, form a 5- to 8-membered carbocyclic ring **[,]** or a 5- to 8-membered **[heterocyclic]** **heterocyclo** or heteroaryl ring **comprising** **[containing]** one or two heteroatoms **independently selected from the group consisting of** **[that are]** nitrogen, oxygen, **and** **[or]** sulfur; **[, with the proviso that]**

as to R^9:

R^9 is selected from the group consisting of hydrido, hydroxy, C_1-C_6-alkyl, C_1-C_6-alkanoyl, aroyl, aryl, ar-C_1-C_6-alkyl, heteroaryl, heteroar-C_1-C_6-alkyl, C_2-C_6-alkynyl, C_2-C_6-alkenyl, thiol-C_1-C_6-alkyl, C_1-C_6-alkylthio-C_1-C_6-alkyl,

cycloalkyl, cycloalkyl-C_1-C_6-alkyl, heterocyclo-C_1-C_6-alkyl, C_1-C_6-alkoxy-C_1-C_6-alkyl, aralkoxy-C_1-C_6-alkyl, C_1-C_6-alkoxy-C_1-C_6-alkoxy-C_1-C_6-alkyl, hydroxy-C_1-C_6-alkyl, hydroxycarbonyl-C_1-C_6-alkyl, hydroxycarbonylar-C_1-C_6-alkyl, aminocarbonyl-C_1-C_6-alkyl, aryloxy-C_1-C_6-alkyl, heteroaryloxy-C_1-C_6-alkyl, arylthio-C_1-C_6-alkyl, heteroarylthio-C_1-C_6-alkyl, a sulfoxide of any of said thio substituents, a sulfone of any said thio substituents, perfluoro-C_1-C_6-alkyl, trifluoromethyl-C_1-C_6-alkyl, halo-C_1-C_6-alkyl, alkoxycarbonylamino-C_1-C_6-alkyl, and amino-C_1-C_6-alkyl, wherein:

the aminoalkyl nitrogen optionally is substituted with up to two substituents independently selected from the group consisting of C_1-C_6-alkyl, ar-C_1-C_6-alkyl, cycloalkyl, and C_1-C_6-alkanoyl,

R^9 and R^8, together with the carbon to which they are bonded, form a carbonyl group, a 5- to 8-membered carbocyclic ring, or a 5- to 8-membered heterocyclo or heteroaryl ring comprising one or two heteroatoms independently selected from the group consisting of nitrogen, oxygen, and sulfur;

as to R^{10}:

R^{10} is selected from the group consisting of hydrido, hydroxy, C_1-C_6-alkyl, C_1-C_6-alkanoyl, aroyl, aryl, ar-C_1-C_6-alkyl, heteroaryl, heteroar-C_1-C_6-alkyl, C_2-C_6-alkynyl, C_2-C_6-alkenyl, thiol-C_1-C_6-alkyl, C_1-C_6-alkylthio-C_1-C_6-alkyl, cycloalkyl, cycloalkyl-C_1-C_6-alkyl, heterocyclo-C_1-C_6-alkyl, C_1-C_6-alkoxy-C_1-C_6-alkyl, aralkoxy-C_1-C_6-alkyl, C_1-C_6-alkoxy-C_1-C_6-alkoxy-C_1-C_6-alkyl, hydroxy-C_1-C_6-alkyl, hydroxycarbonyl-C_1-C_6-alkyl, hydroxycarbonylar-C_1-C_6-alkyl, aminocarbonyl-C_1-C_6-alkyl, aryloxy-C_1-C_6-alkyl, heteroaryloxy-C_1-C_6-alkyl, arylthio-C_1-C_6-alkyl, heteroarylthio-C_1-C_6-alkyl, a sulfoxide of any of said thio substituents, a sulfone of any said thio substituents, perfluoro-C_1-C_6-alkyl,

trifluoromethyl-C_1-C_6-alkyl, halo-C_1-C_6-alkyl, alkoxycarbonylamino-C_1-C_6-alkyl, and amino-C_1-C_6-alkyl, wherein:

the aminoalkyl nitrogen optionally is substituted with up to two substituents independently selected from the group consisting of C_1-C_6-alkyl, ar-C_1-C_6-alkyl, cycloalkyl, and C_1-C_6-alkanoyl,

R^{10} and R^{11}, together with the carbon to which they are bonded, form a carbonyl group, or

R^{10} and R^8 or R^{10} and R^{11}, together with the atom(s) to which they are bonded, form a 5- to 8-membered carbocyclic ring or a 5- to 8-membered heterocyclo or heteroaryl ring comprising one or two heteroatoms independently selected from the group consisting of nitrogen, oxygen, and sulfur;

as to R^{11}:

R^{11} is selected from the group consisting of hydrido, hydroxy, C_1-C_6-alkyl, C_1-C_6-alkanoyl, aroyl, aryl, ar-C_1-C_6-alkyl, heteroaryl, heteroar-C_1-C_6-alkyl, C_2-C_6-alkynyl, C_2-C_6-alkenyl, thiol-C_1-C_6-alkyl, C_1-C_6-alkylthio-C_1-C_6-alkyl, cycloalkyl, cycloalkyl-C_1-C_6-alkyl, heterocyclo-C_1-C_6-alkyl, C_1-C_6-alkoxy-C_1-C_6-alkyl, aralkoxy-C_1-C_6-alkyl, C_1-C_6-alkoxy-C_1-C_6-alkoxy-C_1-C_6-alkyl, hydroxy-C_1-C_6-alkyl, hydroxycarbonyl-C_1-C_6-alkyl, hydroxycarbonylar-C_1-C_6-alkyl, aminocarbonyl-C_1-C_6-alkyl, aryloxy-C_1-C_6-alkyl, heteroaryloxy-C_1-C_6-alkyl, arylthio-C_1-C_6-alkyl, heteroarylthio-C_1-C_6-alkyl, a sulfoxide of any of said thio substituents, a sulfone of any said thio substituents, perfluoro-C_1-C_6-alkyl, trifluoromethyl-C_1-C_6-alkyl, halo-C_1-C_6-alkyl, alkoxycarbonylamino-C_1-C_6-alkyl, and amino-C_1-C_6-alkyl, wherein:

the aminoalkyl nitrogen optionally is substituted with up to two substituents independently selected from the group consisting of C_1-C_6-alkyl, ar-C_1-C_6-alkyl, cycloalkyl, and C_1-C_6-alkanoyl,

R^{11} and R^{10}, together with the carbon to which they are bonded, form a carbonyl group, a 5- to 8-membered carbocyclic ring, or a 5- to 8-membered heterocyclo or heteroaryl ring comprising one or two heteroatoms independently selected from the group consisting of nitrogen, oxygen, and sulfur;

only one of R^8 and R^9 or R^{10} and R^{11} is hydroxy;

[R^{12} and $R^{12'}$ are independently selected from the group consisting of a hydrido, C_1-C_6-alkyl, aryl, ar-C_1-C_6-alkyl, heteroaryl, heteroaralkyl, C_2-C_6-alkynyl, C_2-C_6-alkenyl, thiol-C_1-C_6-alkyl, cycloalkyl, cycloalkyl-C_1-C_6-alkyl, heterocycloalkyl-C_1-C_6-alkyl, C_1-C_6-alkoxy-C_1-C_6-alkyl, aryloxy-C_1-C_6-alkyl, amino-C_1-C_6-alkyl, C_1-C_6-alkoxy-C_1-C_6-alkoxy-C_1-C_6-alkyl, hydroxy-C_1-C_6-alkyl, hydroxycarbonyl-C_1-C_6-alkyl, hydroxycarbonylar-C_1-C_6-alkyl, aminocarbonyl-C_1-C_6-alkyl, aryloxy-C_1-C_6-alkyl, heteroaryloxy-C_1-C_6-alkyl, C_1-C_6-alkylthio-C_1-C_6-alkyl, arylthio-C_1-C_6-alkyl, heteroarylthio-C_1-C_6-alkyl, the sulfoxide or sulfone of any said thio substituents, perfluoro-C_1-C_6-alkyl, trifluoromethyl-C_1-C_6-alkyl, halo-C_1-C_6-alkyl, alkoxycarbonylamino-C_1-C_6-alkyl and an amino-C_1-C_6-alkyl group wherein the aminoalkyl nitrogen is (i) unsubstituted or (ii) substituted with one or two radicals independently selected from the group consisting of C_1-C_6-alkyl, ar-C_1-C_6-alkyl, cycloalkyl and C_1-C_6-alkanoyl;

R^{13} is selected from the group consisting of a hydrido, benzyl, phenyl, C_1-C_6-alkyl, C_2-C_6-alkynyl, C_2-C_6-alkenyl, and a C_1-C_6-hydroxyalkyl group; and]

-G-A-R-E-Y is a substituent that:

has a length greater than that of a pentyl group **and [has a length that is]** less than that of an icosyl group, **and [wherein]**

comprises at least two ring structures;

G is **[an]** aryl or heteroaryl **[group]**;

A is selected from the group consisting of:

(1) –O-, **[;]**

(2) -S-, **[;]**

(3) -NR^{17}-, [;]

(4) -CO-$N(R^{17})$, [or]

(5) -$N(R^{17})$-CO-, [wherein R^{17} is hydrogen, C_1-C_4-alkyl, or phenyl;]

(6) [(5)] -CO-O-, [or]

(7) -O-CO-, [;]

(8) [(6)] -O-CO-O-, [;]

(9) [(7)] -HC=CH-, [;]

(10) [(8)] -NH-CO-NH-, [;]

(11) [(9)] -C≡C-, [;]

(12) [(10)] -NH-CO-O-, [or]

(13) -O-CO-NH-, [;]

(14) [(11)] -N=N-, [;]

(15) [(12)] -NH-NH-, [; and]

(16) [(13)] -CS-$N(R^{18})$-, [or]

(17) -$N(R^{18})$-CS-, [wherein R^{18} is hydrogen C_1-C_4-alkyl, or phenyl; or]

(18) [(14) A is absent and G is bonded directly to R] a bond;

R^{17} is selected from the group consisting of hydrogen, C_1-C_4-alkyl, and phenyl;

R^{18} is selected from the group consisting of hydrogen, C_1-C_4-alkyl, and phenyl;

R is [a moiety] selected from the group consisting of alkyl, alkoxyalkyl, aryl, heteroaryl, cycloalkyl, [heterocycloalkyl] heterocyclo, aralkyl, heteroaralkyl, [heterocycloalkylalkyl] heterocycloalkyl, cycloalkylalkyl, [cycloalkoxyalkyl] cycloalkyloxyalkyl, heterocycloalkoxyalkyl, aryloxyalkyl, heteroaryloxyalkyl, arylthioalkyl, heteroarylthioalkyl, cycloalkylthioalkyl, and [a heterocycloalkylthioalkyl group] heterocyclothioalkyl, wherein:

the aryl, [or] heteroaryl, [or] cycloalkyl, or [heterocycloalkyl] heterocyclo optionally [substituent] is [(i) unsubstituted or (ii)] substituted with up to [one or] two substituents independently [radicals] selected from the group consisting of [a] halo, alkyl, perfluoroalkyl, perfluoroalkoxy, perfluoroalkylthio, trifluoromethylalkyl, amino, alkoxycarbonylalkyl, alkoxy, C_1-C_2-alkylene-dioxy, hydroxycarbonylalkyl,

hydroxycarbonylalkylamino, nitro, hydroxy, hydroxyalkyl, alkanoylamino, and **[a]** alkoxycarbonyl **[group, and R is other than alkyl or alkoxyalkyl when A is -O- or -S-]**;

E is selected from the group consisting of**:**

(1) $-CO(R^{19})-$**,** **[or]**

(2) $-(R^{19})CO-$, **[wherein R^{19} is a heterocycloalkyl, or a cycloalkyl group]**

(3) **[(2)]** $-CONH-$**,** **[or]**

(4) $-HNCO-$**,** **[; and]**

(5) **[(3)]** $-CO-$**,** **[;]**

(6) **[(4)]** $-SO_2-R^{19}-$**,** **[or]**

(7) $-R^{19}-SO_2-$**,** **[;]**

(8) **[(5)]** $-SO_2-$**,** **[;]**

(9) **[(6)]** $-NH-SO_2-$**,** **[or]**

(10) $-SO_2-NH-$**, and** **[; or]**

(11) **[(7)** **E is absent and R is bonded directly to Y]** **a bond**; **[and]**

R^{19} is selected from the group consisting of heterocyclo and cycloalkyl; and

Y is **[absent or is]** selected from the group consisting of **[a]** hydrido, alkyl, alkoxy, haloalkyl, aryl, aralkyl, cycloalkyl, heteroaryl, hydroxy, aryloxy, aralkoxy, heteroaryloxy, heteroaralkyl, perfluoroalkoxy, perfluoroalkylthio, trifluoromethylalkyl, alkenyl, **[heterocycloalkyl]** **heterocyclo**, cycloalkyl, trifluoromethyl, alkoxycarbonyl, and **[a]** aminoalkyl **[group]**, wherein**:**

the aryl**,** **[or]** heteroaryl**,** or **heterocyclo optionally** **[heterocycloalkyl group]** is **[(i) unsubstituted or (ii)]** substituted with **up to** **[one or]** two **substituents** **[radicals]** independently selected from the group consisting of **[an]** alkanoyl, halo, nitro, aralkyl, aryl, alkoxy, and **[an]** amino**,** **[group]** wherein**:**

the amino nitrogen **optionally** is **[(i) unsubstituted or (ii)]** substituted with **up to** **[one or]** two **substituents** **[groups]** independently selected from **the group consisting of** hydrido, alkyl, and **[an]** aralkyl **[group]**.

53. **(amended once)** The compound or salt according to claim 52, wherein **[said]** -G-A-R-E-Y **[substituent contains]** **comprises** two to four **ring structures independently selected from the group consisting of cycloalkyl, aryl, heterocyclo, and heteroaryl** **[carbocyclic or heterocyclic rings]**.

54. **(amended once)** The compound or salt according to claim 52, wherein each of the two to four **ring structures** **[rings]** is 6-membered.

55. **(amended once)** The compound or salt according to claim 52, wherein **[said]** -G-A-R-E-Y **[substituent]** has a length that is greater than **that of** a hexyl group and **[a length that is]** less than that of a stearyl group.

57. **(amended once)** The compound or salt according to claim 52, , wherein R is **[an]** aryl, heteroaryl, cycloalkyl, or **heterocyclo** **[heterocycloalkyl group]**.

58. **(amended once)** The compound or salt according to claim 52, wherein E is absent.

59. **(amended once)** The compound or salt according to claim 52, wherein Y is selected from the group consisting of hydrido, **[an]** alkyl, alkoxy, perfluoroalkoxy, and **[a]** perfluoroalkylthio **[group]**.

60. **(amended once)** The compound or salt according to claim 52, wherein R^{14} is hydrido.

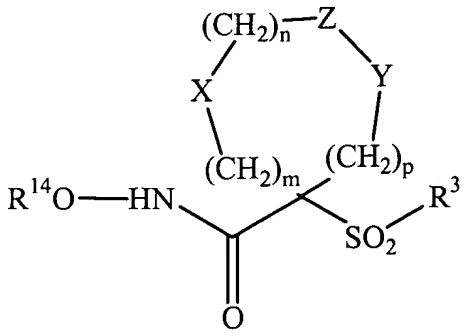
61. **(amended once)** The compound or salt according to claim 52, wherein:

W **[of the C(W)R^{15}]** is O; and

R^{15} is **[a]** C_1-C_6-alkyl, aryl, C_1-C_6-alkoxy, heteroaryl-C_1-C_6-alkyl, C_3-C_8-cycloalkyl-C_1-C_6-alkyl, or aryloxy **[group]**.

62. **(amended once)** A compound **or a salt thereof, wherein:**

the compound corresponds [corresponding] in structure to formula III**: [, below, or a pharmaceutically acceptable salt thereof]**



III

[wherein]

R^3 is a single-ringed aryl or heteroaryl group that is 5- or 6-membered, and is itself substituted at its own 4-position when a 6-membered ring **or [and]** at its own 3- or 4-position when a 5-membered ring with a substituent selected from the group consisting of **[a]** thiophenoxy, 4-chloro-phenoxy, 3-chlorophenoxy, 4-methoxyphenoxy, 3-benzodioxol-5-yloxy, 3,4-dimethylphenoxy, 4-fluorophenoxy, 4-fluorothiophenoxy, phenoxy, 4-trifluoromethoxyphenoxy, 4-trifluoromethylphenoxy, 4-(trifluoromethylthio)phenoxy, 4-(trifluoromethylthio)thiophenoxy, 4-chloro-3-fluorophenoxy, 4-isopropoxyphenoxy, 4-isopropylphenoxy, (2-methyl-1,3-benzothiazol-5-yl)oxy, 4-(1H-imidazol-1-yl)phenoxy, 4-chloro-3-methylphenoxy, 3-methyl-phenoxy, 4-ethoxyphenoxy, 3,4-difluorophenoxy, 4-chloro-3-methylphenoxy, 4-fluoro-3-chlorophenoxy, 4-(1H-1,2,4-triazol-1-yl)phenoxy, 3,5-difluorophenoxy, 3,4-dichlorophenoxy, 4-cyclopentylphenoxy, 4-bromo-3-methylphenoxy, 4-bromophenoxy, 4-methylthiophenoxy, 4-phenylphenoxy, 4-benzylphenoxy, 6-quinolinyloxy, 4-amino-3-methylphenoxy, 3-methoxyphenoxy, 5,6,7,8-tetrahydro-2-naphthalenyloxy, 3-hydroxymethylphenoxy, and **[a]** 4-benzyloxyphenoxy **[group]**;

R^{14} is hydrido, a pharmaceutically acceptable cation, or $C(W)R^{15}$; **[where]**

W is O or S; **[and]**

R^{15} is selected from the group consisting of **[a]** C_1-C_6-alkyl, aryl, C_1-C_6-alkoxy, heteroaryl-C_1-C_6-alkyl, C_3-C_8-cycloalkyl-C_1-C_6-alkyl, aryloxy, ar-C_1-C_6-alkoxy, ar-C_1-C_6-alkyl, heteroaryl, and amino-C_1-C_6-alkyl, **[group]** wherein the amino-**C_1-C_6-**alkyl nitrogen **optionally** is **[(i) unsubstituted or (ii)]** substituted with:

up to **[one or]** two substituents independently selected from the group consisting of **[an]** C_1-C_6-alkyl, aryl, ar-C_1-C_6-alkyl, C_3-C_8-cycloalkyl-C_1-C_6-alkyl, ar-C_1-C_6-alkoxycarbonyl, C_1-C_6-alkoxycarbonyl, and C_1-C_6-alkanoyl **[radical]**, or **[(iii) wherein the amino C_1-C_6-alkyl nitrogen and]**

two substituents **such that the two substituents, together with the amino-C_1-C_6-alkyl nitrogen, [attached thereto]** form a 5- to 8-membered heterocyclo or heteroaryl ring;

m is zero, 1, or 2;

n is zero, 1, or 2;

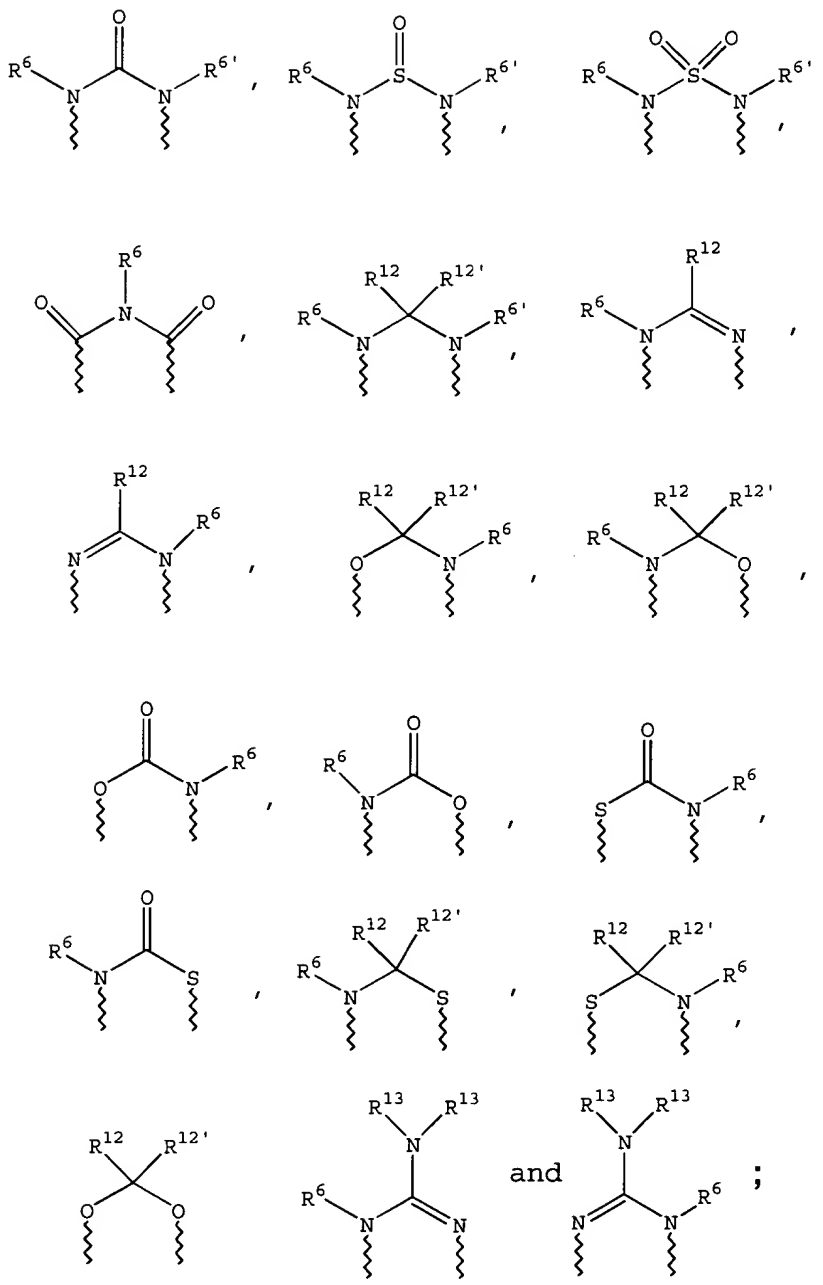
p is zero, 1, or 2;

the sum of m + n + p = **[1,]** 2 **[, 3 or 4]**;

[(a)] one of X, Y, and Z is **[selected from the group consisting of C(O), NR^6,]** O, **[S, S(O), $S(O)_2$, and $NS(O)_2R^7$,]** and the remaining two of X, Y, and Z are CR^8R^9 **[,]** and $CR^{10}R^{11}$ **[, or**

(b) X and Z or Z and Y together constitute a moiety that is selected from the group consisting of $NR^6C(O)$, $NR^6S(O)$, $NR^6S(O)_2$, NR^6S, NR^6O, SS, NR^6NR^6 and OC(O), with the remaining one of X, Y, and Z being CR^8R^9, or

(c) n is zero and X, Y and Z together constitute a moiety selected from the group consisting of



wherein wavy lines are bonds to the atoms of the depicted ring;

R^6 and $R^{6'}$ are independently selected from the group consisting of hydrido, C_1-C_6-alkanoyl, C_6-aryl-C_1-C_6-alkyl, aroyl, bis(C_1-C_6-alkoxy-C_1-C_6-alkyl)-C_1-C_6-alkyl, C_1-C_6-alkyl, C_1-C_6-haloalkyl, C_1-C_6-perfluoroalkyl, C_1-C_6-trifluoromethylalkyl, C_1-C_6-perfluoroalkoxy-C_1-C_6-alkyl, C_1-C_6-alkoxy-C_1-C_6-alkyl, C_3-C_6-cycloalkyl, C_3-C_8-heterocycloalkyl, C_3-C_8-heterocycloalkylcarbonyl, C_6-aryl, C_5-C_6-heterocyclo, C_5-C_6-

heteroaryl, C_3-C_8-cycloalkyl-C_1-C_6-alkyl, C_6-aryloxy-C_1-C_6-alkyl, heteroaryloxy-C_1-C_6-alkyl, heteroaryl-C_1-C_6-alkoxy-C_1-C_6-alkyl, heteroarylthio-C_1-C_6-alkyl, C_6-arylsulfonyl, C_1-C_6-alkylsulfonyl, C_5-C_6-heteroarylsulfonyl, carboxy-C_1-C_6-alkyl, C_1-C_4-alkoxycarbonyl-C_1-C_6-alkyl, aminocarbonyl, C_1-C_6-alkyliminocarbonyl, C_6-aryliminocarbonyl, C_5-C_6-heterocycloiminocarbonyl, C_6-arylthio-C_1-C_6-alkyl, C_1-C_6-alkylthio-C_1-C_6-alkyl, C_6-arylthio-C_3-C_6-alkenyl, C_1-C_4-alkylthio-C_3-C_6-alkenyl, C_5-C_6-heteroaryl-C_1-C_6-alkyl, halo-C_1-C_6-alkanoyl, hydroxy-C_1-C_6-alkanoyl, thiol-C_1-C_6-alkanoyl, C_3-C_6-alkenyl, C_3-C_6-alkynyl, C_1-C_4-alkoxy-C_1-C_4-alkyl, C_1-C_5-alkoxycarbonyl, aryloxycarbonyl, NR^8R^9-C_1-C_5-alkylcarbonyl, hydroxy-C_1-C_5-alkyl, an aminocarbonyl wherein the aminocarbonyl nitrogen is (i) unsubstituted or (ii) substituted with one or two radicals independently selected from the group consisting of C_1-C_6-alkyl, ar-C_1-C_6-alkyl, C_3-C_8-cycloalkyl, and a C_1-C_6-alkanoyl group, hydroxyaminocarbonyl, an aminosulfonyl group wherein the aminosulfonyl nitrogen is (i) unsubstituted or (ii) substituted with one or two radicals independently selected from the group consisting of C_1-C_6-alkyl, ar-C_1-C_6-alkyl, C_3-C_8-cycloalkyl, and a C_1-C_6-alkanoyl group, an amino-C_1-C_6-alkylsulfonyl group wherein the amino-C_1-C_6-alkylsulfonyl nitrogen is (i) unsubstituted or (ii) substituted with one or two radicals independently selected from the group consisting of C_1-C_6-alkyl, ar-C_1-C_6-alkyl, C_3-C_8-cycloalkyl, and a C_1-C_6-alkanoyl group and an amino-C_1-C_6-alkyl group wherein the aminoalkyl nitrogen is (i) unsubstituted or (ii) substituted with one or two radicals independently selected from the group consisting of C_1-C_6-alkyl, ar-C_1-C_6-alkyl, C_3-C_8-cycloalkyl, and a C_1-C_6-alkanoyl group;

R^7 is selected from the group consisting of a arylalkyl, aryl, heteroaryl, heterocyclo, C_1-C_6-alkyl, C_3-C_6-alkynyl, C_3-C_6-alkenyl, C_1-C_6-carboxyalkyl, and a C_1-C_6-hydroxyalkyl group];

<u>as to R^8:</u>

R^8 **is** **[and R^9 and R^{10} and R^{11} are independently]** selected from the group consisting of **[a]** hydrido, hydroxy, C_1-C_6-alkyl, C_1-C_6-alkanoyl, aroyl, aryl, ar-C_1-C_6-alkyl, heteroaryl, heteroar-C_1-C_6-alkyl, C_2-C_6-alkynyl, C_2-C_6-alkenyl, thiol-C_1-C_6-alkyl, C_1-C_6-alkylthio-C_1-C_6-alkyl, cycloalkyl, cycloalkyl-C_1-C_6-alkyl, **[heterocycloalkyl-C_1-C_6-alkyl]** **heterocyclo-C_1-C_6-alkyl**, C_1-C_6-alkoxy-C_1-C_6-alkyl, aralkoxy-C_1-C_6-alkyl, C_1-C_6-alkoxy-C_1-C_6-alkoxy-C_1-C_6-alkyl, hydroxy-C_1-C_6-alkyl, hydroxycarbonyl-C_1-C_6-alkyl, hydroxycarbonylar-C_1-C_6-alkyl, aminocarbonyl-C_1-C_6-alkyl, aryloxy-C_1-C_6-alkyl, heteroaryloxy-C_1-C_6-alkyl, arylthio-C_1-C_6-alkyl, heteroarylthio-C_1-C_6-alkyl, **a** **[the]** sulfoxide **[or sulfone]** of any of said thio substituents, **a sulfone of any said thio substituents,** perfluoro-C_1-C_6-alkyl, trifluoromethyl-C_1-C_6-alkyl, halo-C_1-C_6-alkyl, alkoxycarbonylamino-C_1-C_6-alkyl, and **[an]** amino-C_1-C_6-alkyl, **[group]** wherein:

the aminoalkyl nitrogen **optionally** is **[(i) unsubstituted or (ii)]** substituted with **up to** **[one or]** two **substituents** **[radicals]** independently selected from the group consisting of C_1-C_6-alkyl, ar-C_1-C_6-alkyl, cycloalkyl, and C_1-C_6-alkanoyl, **[or wherein]**

R^8 and R^9, **together with** **[or R^{10} and R^{11} and]** the carbon to which they are bonded, form a carbonyl group, or **[wherein]**

R^8 and R^9 or **[R^{10} and R^{11}, or]** R^8 and R^{10}, together with the **atom(s)** **[atoms]** to which they are bonded, form a 5- to 8-membered carbocyclic ring **[,]** or a 5- to 8-membered **[heterocyclic]** **heterocyclo** or heteroaryl ring **comprising** **[containing]** one or two heteroatoms **independently selected from the group consisting of** **[that are]** nitrogen, oxygen, **and** **[or]** sulfur; **[, with the proviso that]**

as to R^9:

R^9 is selected from the group consisting of hydrido, hydroxy, C_1-C_6-alkyl, C_1-C_6-alkanoyl, aroyl, aryl, ar-C_1-C_6-alkyl, heteroaryl, heteroar-C_1-C_6-alkyl, C_2-C_6-alkynyl, C_2-C_6-alkenyl, thiol-C_1-C_6-alkyl, C_1-C_6-alkylthio-C_1-C_6-alkyl,

cycloalkyl, cycloalkyl-C_1-C_6-alkyl, heterocyclo-C_1-C_6-alkyl, C_1-C_6-alkoxy-C_1-C_6-alkyl, aralkoxy-C_1-C_6-alkyl, C_1-C_6-alkoxy-C_1-C_6-alkoxy-C_1-C_6-alkyl, hydroxy-C_1-C_6-alkyl, hydroxycarbonyl-C_1-C_6-alkyl, hydroxycarbonylar-C_1-C_6-alkyl, aminocarbonyl-C_1-C_6-alkyl, aryloxy-C_1-C_6-alkyl, heteroaryloxy-C_1-C_6-alkyl, arylthio-C_1-C_6-alkyl, heteroarylthio-C_1-C_6-alkyl, a sulfoxide of any of said thio substituents, a sulfone of any said thio substituents, perfluoro-C_1-C_6-alkyl, trifluoromethyl-C_1-C_6-alkyl, halo-C_1-C_6-alkyl, alkoxycarbonylamino-C_1-C_6-alkyl, and amino-C_1-C_6-alkyl, wherein:

the aminoalkyl nitrogen optionally is substituted with up to two substituents independently selected from the group consisting of C_1-C_6-alkyl, ar-C_1-C_6-alkyl, cycloalkyl, and C_1-C_6-alkanoyl,

R^9 and R^8, together with the carbon to which they are bonded, form a carbonyl group, a 5- to 8-membered carbocyclic ring, or a 5- to 8-membered heterocyclo or heteroaryl ring comprising one or two heteroatoms independently selected from the group consisting of nitrogen, oxygen, and sulfur;

as to R^{10}:

R^{10} is selected from the group consisting of hydrido, hydroxy, C_1-C_6-alkyl, C_1-C_6-alkanoyl, aroyl, aryl, ar-C_1-C_6-alkyl, heteroaryl, heteroar-C_1-C_6-alkyl, C_2-C_6-alkynyl, C_2-C_6-alkenyl, thiol-C_1-C_6-alkyl, C_1-C_6-alkylthio-C_1-C_6-alkyl, cycloalkyl, cycloalkyl-C_1-C_6-alkyl, heterocyclo-C_1-C_6-alkyl, C_1-C_6-alkoxy-C_1-C_6-alkyl, aralkoxy-C_1-C_6-alkyl, C_1-C_6-alkoxy-C_1-C_6-alkoxy-C_1-C_6-alkyl, hydroxy-C_1-C_6-alkyl, hydroxycarbonyl-C_1-C_6-alkyl, hydroxycarbonylar-C_1-C_6-alkyl, aminocarbonyl-C_1-C_6-alkyl, aryloxy-C_1-C_6-alkyl, heteroaryloxy-C_1-C_6-alkyl, arylthio-C_1-C_6-alkyl, heteroarylthio-C_1-C_6-alkyl, a sulfoxide of any of said thio substituents, a sulfone of any said thio substituents, perfluoro-C_1-C_6-alkyl,

trifluoromethyl-C_1-C_6-alkyl, halo-C_1-C_6-alkyl, alkoxycarbonylamino-C_1-C_6-alkyl, and amino-C_1-C_6-alkyl, wherein:

the aminoalkyl nitrogen optionally is substituted with up to two substituents independently selected from the group consisting of C_1-C_6-alkyl, ar-C_1-C_6-alkyl, cycloalkyl, and C_1-C_6-alkanoyl,

R^{10} and R^{11}, together with the carbon to which they are bonded, form a carbonyl group, or

R^{10} and R^8 or R^{10} and R^{11}, together with the atom(s) to which they are bonded, form a 5- to 8-membered carbocyclic ring or a 5- to 8-membered heterocyclo or heteroaryl ring comprising one or two heteroatoms independently selected from the group consisting of nitrogen, oxygen, and sulfur;

as to R^{11}:

R^{11} is selected from the group consisting of hydrido, hydroxy, C_1-C_6-alkyl, C_1-C_6-alkanoyl, aroyl, aryl, ar-C_1-C_6-alkyl, heteroaryl, heteroar-C_1-C_6-alkyl, C_2-C_6-alkynyl, C_2-C_6-alkenyl, thiol-C_1-C_6-alkyl, C_1-C_6-alkylthio-C_1-C_6-alkyl, cycloalkyl, cycloalkyl-C_1-C_6-alkyl, heterocyclo-C_1-C_6-alkyl, C_1-C_6-alkoxy-C_1-C_6-alkyl, aralkoxy-C_1-C_6-alkyl, C_1-C_6-alkoxy-C_1-C_6-alkoxy-C_1-C_6-alkyl, hydroxy-C_1-C_6-alkyl, hydroxycarbonyl-C_1-C_6-alkyl, hydroxycarbonylar-C_1-C_6-alkyl, aminocarbonyl-C_1-C_6-alkyl, aryloxy-C_1-C_6-alkyl, heteroaryloxy-C_1-C_6-alkyl, arylthio-C_1-C_6-alkyl, heteroarylthio-C_1-C_6-alkyl, a sulfoxide of any of said thio substituents, a sulfone of any said thio substituents, perfluoro-C_1-C_6-alkyl, trifluoromethyl-C_1-C_6-alkyl, halo-C_1-C_6-alkyl, alkoxycarbonylamino-C_1-C_6-alkyl, and amino-C_1-C_6-alkyl, wherein:

the aminoalkyl nitrogen optionally is substituted with up to two substituents independently selected from the group consisting of C_1-C_6-alkyl, ar-C_1-C_6-alkyl, cycloalkyl, and C_1-C_6-alkanoyl,

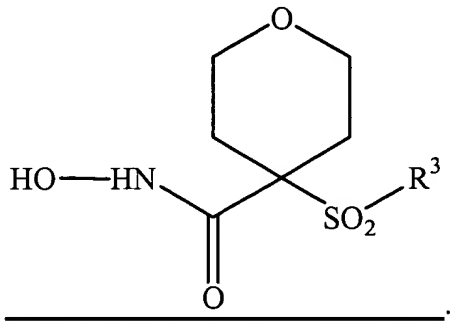
R^{11} and R^{10}, together with the carbon to which they are bonded, form a carbonyl group, a 5- to 8-membered carbocyclic ring, or a 5- to 8-membered heterocyclo or heteroaryl ring comprising one or two heteroatoms independently selected from the group consisting of nitrogen, oxygen, and sulfur; and

only one of R^8 and R^9 or R^{10} and R^{11} is hydroxy **[;**

R^{12} and $R^{12'}$ are independently selected from the group consisting of a hydrido, C_1-C_6-alkyl, aryl, ar-C_1-C_6-alkyl, heteroaryl, heteroaralkyl, C_2-C_6-alkynyl, C_2-C_6-alkenyl, thiol-C_1-C_6-alkyl, cycloalkyl, cycloalkyl-C_1-C_6-alkyl, heterocycloalkyl-C_1-C_6-alkyl, C_1-C_6-alkoxy-C_1-C_6-alkyl, aryloxy-C_1-C_6-alkyl, amino-C_1-C_6-alkyl, C_1-C_6-alkoxy-C_1-C_6-alkoxy-C_1-C_6-alkyl, hydroxy-C_1-C_6-alkyl, hydroxycarbonyl-C_1-C_6-alkyl, hydroxycarbonylar-C_1-C_6-alkyl, aminocarbonyl-C_1-C_6-alkyl, aryloxy-C_1-C_6-alkyl, heteroaryloxy-C_1-C_6-alkyl, C_1-C_6-alkylthio-C_1-C_6-alkyl, arylthio-C_1-C_6-alkyl, heteroarylthio-C_1-C_6-alkyl, the sulfoxide or sulfone of any said thio substituents, perfluoro-C_1-C_6-alkyl, trifluoromethyl-C_1-C_6-alkyl, halo-C_1-C_6-alkyl, alkoxycarbonylamino-C_1-C_6-alkyl, and an amino-C_1-C_6-alkyl group wherein the aminoalkyl nitrogen is (i) unsubstituted or (ii) substituted with one or two radicals independently selected from the group consisting of C_1-C_6-alkyl, ar-C_1-C_6-alkyl, cycloalkyl and C_1-C_6-alkanoyl; and

R^{13} is selected from the group consisting of a hydrido, benzyl, phenyl, C_1-C_6-alkyl, C_2-C_6-alkynyl, C_2-C_6-alkenyl and a C_1-C_6-hydroxyalkyl group].

63. **(amended once)** The compound or salt according to claim 62, wherein the **[sum of m + n + p = 1 or 2]** **compound corresponds in structure to the following formula:**



64. **(amended once)** The compound or salt according to claim **[62]** **63,** wherein **the salt is a pharmaceutically acceptable salt** **[Z is O, S or NR^6]**.

65. **(amended once)** The compound or salt according to claim 62, wherein **the salt is a pharmaceutically acceptable salt** **[R^6 is selected from the group consisting of C_3-C_6-cycloalkyl, C_1-C_6-alkyl, C_3-C_6-alkenyl, C_3-C_6-alkynyl, C_1-C_6-alkoxy-C_1-C_6-alkyl, amino-C_1-C_6-alkyl, aminosulfonyl, heteroaryl-C_1-C_6-alkyl, aryloxycarbonyl, and C_1-C_6-alkoxycarbonyl]**.

67. **(amended once)** The compound or salt according to claim 62, wherein R^{14} is hydrido.

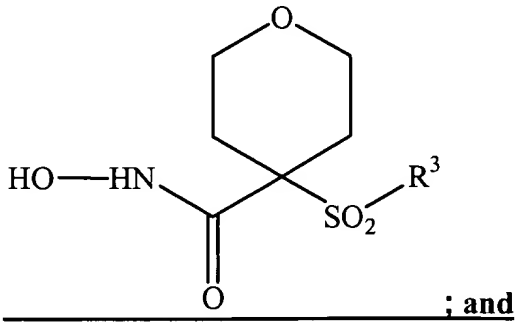
68. **(amended once)** The compound or salt according to claim 62, wherein:

W **[of the $C(W)R^{15}$]** is O; and

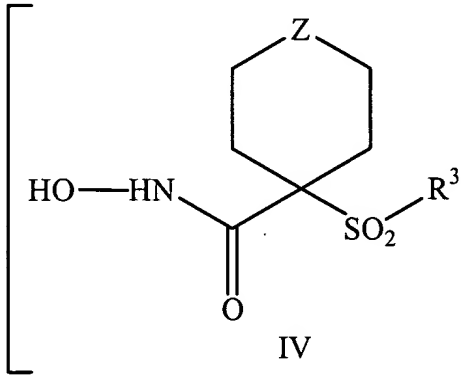
R^{15} is **[a]** C_1-C_6-alkyl, aryl, C_1-C_6-alkoxy, heteroaryl-C_1-C_6-alkyl, C_3-C_8-cycloalkyl-C_1-C_6-alkyl, or aryloxy **[group]**.

69. **(amended once)** A compound **or a salt thereof, wherein:**

the compound corresponds [corresponding] in structure to **the following** formula**: [IV, below, or a pharmaceutically acceptable salt thereof]**



; and



IV

wherein]

R^3 is a **[single-ringed] 5- to 6-membered** aryl or **5- to 6-membered** heteroaryl group **[that is 5- or 6-membered], wherein: [and]**

the aryl or heteroaryl is **[itself]** substituted at its own 4-position when a 6-membered ring or at its own 3- or 4-position when a 5-membered ring with a substituent selected from the group consisting of **[one other]** single-ringed aryl**, single-ringed [or]** heteroaryl **[group, a]** N-piperidyl**, [group, a]** N-piperazinyl**, [group, a]** phenoxy**, [group, a]** thiophenoxy**, [group, a]** 4-thiopyridyl**, [group, a]** phenylazo**, and [group and a]** benzamido **[group; and**

Z is selected group the group consisting of O, S, NR^6, SO, SO_2, and NSO_2R^7,

wherein R^6 is selected from the group consisting of hydrido, C_1-C_5-alkyl, C_1-C_5-alkanoyl, benzyl, benzoyl, C_3-C_5-alkynyl, C_3-C_5-alkenyl, C_1-C_3-alkoxy-C_1-C_4-alkyl, C_3-C_6-cycloalkyl, heteroaryl-C_1-C_6-alkyl, C_1-C_5-hydroxyalkyl, C_1-C_5-carboxyalkyl, C_1-C_5-alkoxy

C_1-C_5-alkylcarbonyl, and NR^8R^9-C_1-C_5-alkylcarbonyl or NR^8R^9-C_1-C_5-alkyl, wherein R^8 and R^9 are independently hydrido, C_1-C_5-alkyl, C_1-C_5-alkoxycarbonyl or aryl-C_1-C_5-alkoxycarbonyl, or NR^8R^9 together form a heterocyclic ring containing 5- to 8-atoms in the ring; and

R^7 is selected from the group consisting of a arylalkyl, aryl, heteroaryl, heterocyclo, C_1-C_6-alkyl, C_3-C_6-alkynyl, C_3-C_6-alkenyl, C_1-C_6-carboxyalkyl, and a C_1-C_6-hydroxyalkyl group].

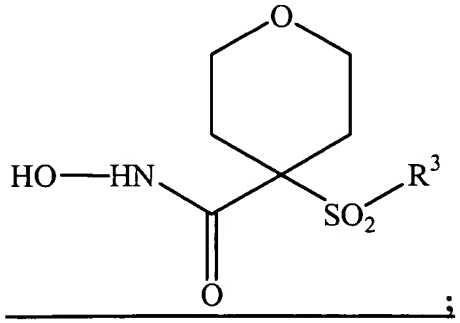
70. **(amended once)** The compound or salt according to claim 69, wherein R^3 has a length that is greater than that of an octyl group and **[a length that is]** less than that of a stearyl group.

71. **(amended once)** The compound or salt according to claim 69, wherein **the salt is a pharmaceutically acceptable salt [Z is O, S or NR^6]**.

Claims 72-81 have been canceled without prejudice to their patentability.

82. **(amended once)** A **[The]** compound or a salt **thereof, [according to claim 69]** wherein: **[said]**

the compound corresponds in structure to the following formula:



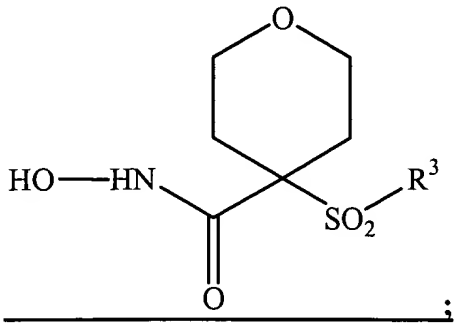
;

R^3 **[group]** is **[a PhR^{23} group, wherein Ph is a]** phenyl **[ring that is]** substituted at its 4-position by **[an]** R^{23}; **[group that is a]**

R^{23} is [substituent] selected from the group consisting of **[another]** single-ringed aryl, **single-ringed [or]** heteroaryl, **[group, a]** piperidyl, **[group, a]** piperazinyl, **[group, a]** phenoxy, **[group, a]** thiophenoxy, **[group, a]** phenylazo, **[group]** and **[a]** benzamido **[group]**.

83. **(amended once)** **A** **[The]** compound or **a** salt **thereof,** **[according to claim 82]** wherein:

the compound corresponds in structure to the following formula:



;

R^3 is phenyl substituted at its 4-position by R^{23}; and

R^{23} is selected from the group consisting of single-ringed aryl, single-ringed heteroaryl, piperidyl, piperazinyl, phenoxy, thiophenoxy, phenylazo, and benzamido, wherein any such group is:

substituted with a **substituent** **[moiety that is]** selected from the group consisting of **[a]** halogen, **[a]** C_1-C_4-alkoxy, **[group, a]** C_1-C_4-alkyl, **[group, a]** dimethylamino, **[group, a]** carboxyl-C_1-C_3-alkylene, **[group, a]** C_1-C_4-alkoxy carbonyl C_1-C_3-alkylene, **[group, a]** trifluoromethylthio, **[group, a]** trifluoromethoxy, **[group, a]** trifluoromethyl, **[group]** and **[a]** carboxamido-C_1-C_3-alkylene **[group]**, or

[is] substituted at the meta- and para-positions by a methylenedioxy group.

84. **(amended once)** The compound or salt according to claim 83, wherein **the** **[said]** R^{23} **single-ringed aryl, single-ringed heteroaryl, piperidyl, piperazinyl, phenoxy, thiophenoxy, phenylazo, or benzamido** **[group]** is substituted at the para-position.

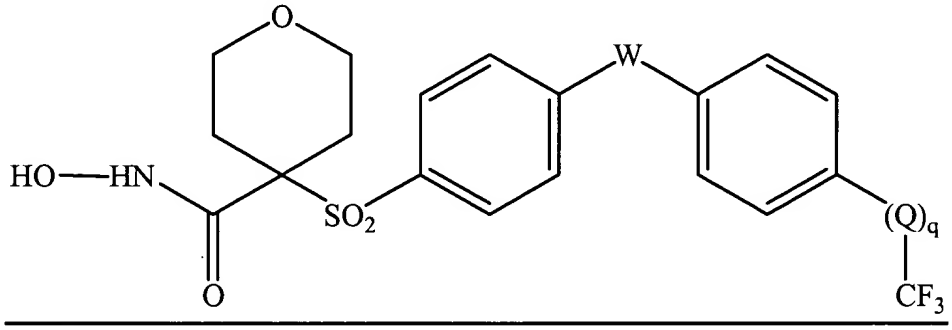
85. **(amended once)** The compound or salt according to claim 84 wherein **[said]** R^{23} **[group]** is phenoxy **that is:**

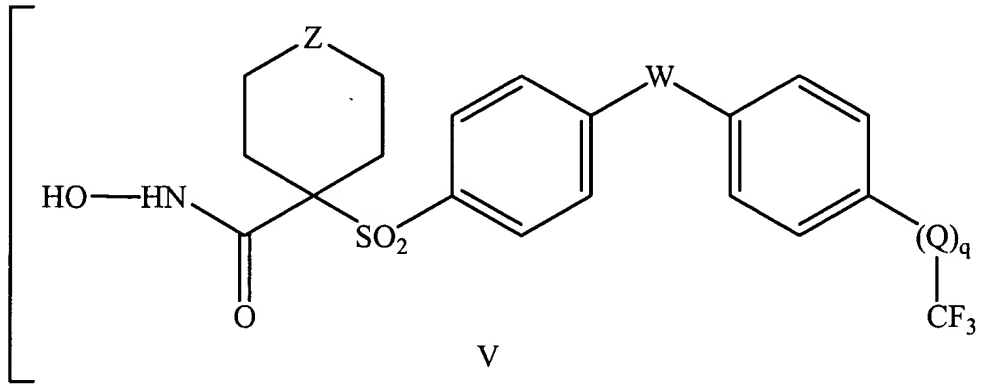
substituted with a substituent selected from the group consisting of halogen, C_1-C_4-alkoxy, C_1-C_4-alkyl, dimethylamino, carboxyl-C_1-C_3-alkylene, C_1-C_4-alkoxy carbonyl C_1-C_3-alkylene, trifluoromethylthio, trifluoromethoxy, trifluoromethyl, and carboxamido-C_1-C_3-alkylene, or

substituted at the meta- and para-positions by a methylenedioxy group.

87. **(amended once)** A compound **or a salt thereof, wherein:**

the compound corresponds [corresponding] in structure to **the following** formula V**: [, below, or a pharmaceutically acceptable salt thereof]**





V

wherein

Z is O, S or NR^6];

W and Q are independently oxygen (O), NR^6, or sulfur (S)**; [,]**

R^6 is selected from the group consisting of C_3-C_6-cycloalkyl, C_1-C_6-alkyl, C_3-C_6-alkenyl, C_3-C_6-alkynyl, C_1-C_6-alkoxy-C_1-C_6-alkyl, amino-C_1-C_6-alkyl, aminosulfonyl, heteroaryl-C_1-C_6-alkyl, aryloxycarbonyl, and C_1-C_6-alkoxycarbonyl; and

q is zero or one such that when q is zero, Q is absent and the trifluoromethyl group is bonded directly to the depicted phenyl ring.

88. **(amended once)** The compound or salt according to claim 87, wherein q is zero.

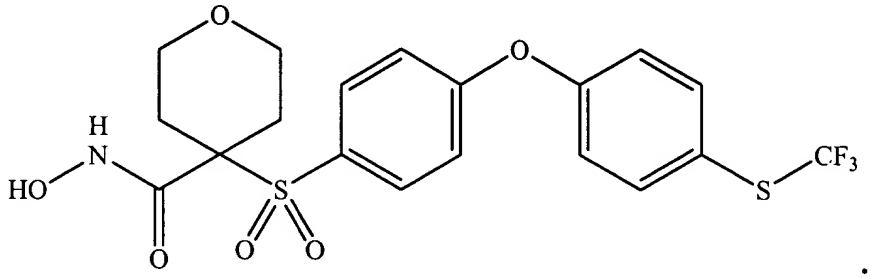
89. **(amended once)** The compound or salt according to claim 87, wherein W is O.

90. **(amended once)** The compound or salt according to claim 89, wherein q is zero.

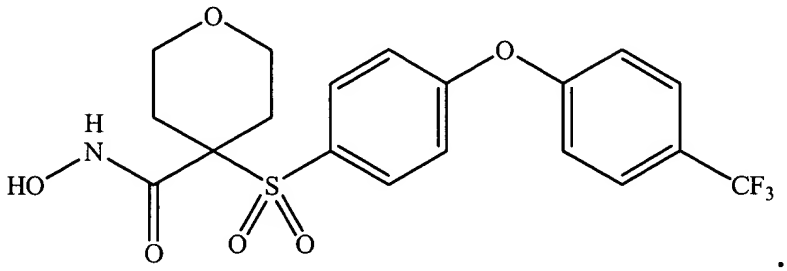
91. **(amended once)** The compound or salt according to claim 89, wherein q is one and Q is O.

92. **(amended once)** The compound or salt according to claim 89, wherein q is one and Q is S.

93. **(amended once)** The compound or salt according to claim 87, wherein said **compound [inhibitor]** corresponds in structure to the formula:



94. **(amended once)** The compound or salt according to claim 87, wherein said **compound [inhibitor]** corresponds in structure to the formula:



128. **(amended once)** A pharmaceutical composition, **wherein the composition [that]** comprises a compound **or pharmaceutically-acceptable salt** according to claim **[52] 149** dissolved or dispersed in a pharmaceutically acceptable carrier.

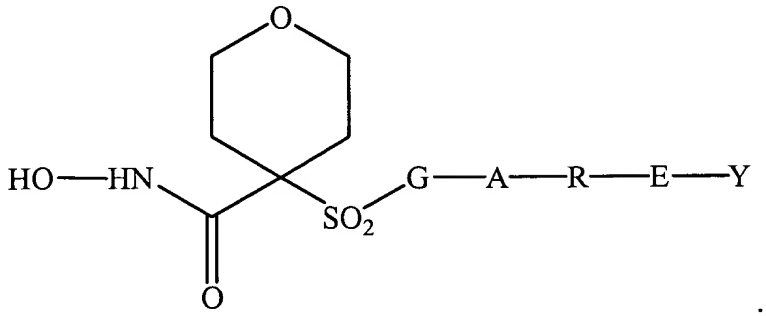
129. **(amended once)** A pharmaceutical composition, **wherein the composition [that]** comprises a compound **or pharmaceutically-acceptable salt** according to claim **[62] 65** dissolved or dispersed in a pharmaceutically acceptable carrier.

130. **(amended once)** A pharmaceutical composition, **wherein the composition [that]** comprises a compound **or pharmaceutically-acceptable salt** according to claim **[69] 71** dissolved or dispersed in a pharmaceutically acceptable carrier.

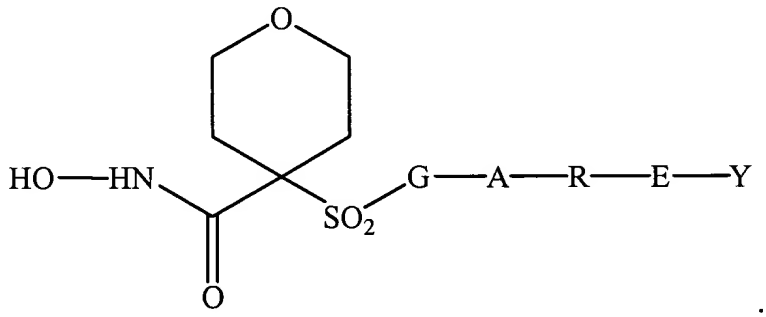
131. **(amended once)** A pharmaceutical composition, **wherein the composition [that]** comprises a compound **or pharmaceutically-acceptable salt** according to claim **[87] 152** dissolved or dispersed in a pharmaceutically acceptable carrier.

The following new claims have been added by this Amendment B:

147. **(new)** The process according to claim 7, wherein the compound corresponds in structure to the formula below:



148. **(new)** The compound or salt according to claim 52, wherein the compound corresponds in structure to the formula below:



149. **(new)** The compound or salt according to claim 52, wherein the salt is a pharmaceutically acceptable salt.

150. **(new)** The compound or salt according to claim 82, wherein the salt is a pharmaceutically acceptable salt.

151. **(new)** The compound or salt according to claim 83, wherein the salt is a pharmaceutically acceptable salt.

152. **(new)** The compound or salt according to claim 87, wherein the salt is a pharmaceutically acceptable salt.

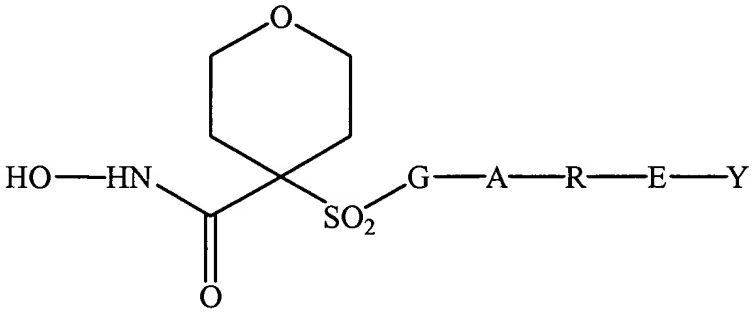
153. **(new)** The compound or salt according to claim 93, wherein the salt is a pharmaceutically acceptable salt.

154. **(new)** A pharmaceutical composition, wherein the composition comprises a compound or pharmaceutically-acceptable salt according to claim 53 dissolved or dispersed in a pharmaceutically acceptable carrier.

155. **(new)** The compound or salt according to claim 94, wherein the salt is a pharmaceutically acceptable salt.

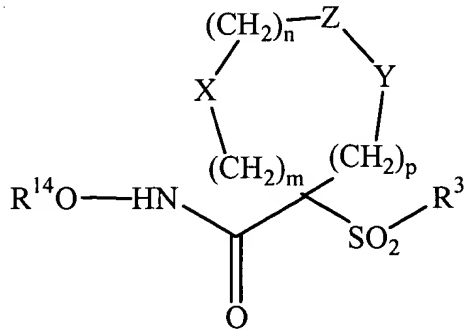
156. **(new)** A pharmaceutical composition, wherein the composition comprises a compound or pharmaceutically-acceptable salt according to claim 155 dissolved or dispersed in a pharmaceutically acceptable carrier.

157. **(new)** A process according to claim 20, wherein the compound corresponds in structure to the formula below:



158. **(new)** A compound or a salt thereof, wherein:

the compound corresponds in structure to formula III:



III

;

R^{14} is hydrido, a pharmaceutically acceptable cation, or $C(W)R^{15}$;

W is O or S;

R^{15} is selected from the group consisting of C_1-C_6-alkyl, aryl, C_1-C_6-alkoxy, heteroaryl-C_1-C_6-alkyl, C_3-C_8-cycloalkyl-C_1-C_6-alkyl, aryloxy, ar-C_1-C_6-alkoxy, ar-C_1-C_6-alkyl, heteroaryl, and amino-C_1-C_6-alkyl, wherein the amino-C_1-C_6-alkyl nitrogen optionally is substituted with:

up to two substituents independently selected from the group consisting of C_1-C_6-alkyl, aryl, ar-C_1-C_6-alkyl, C_3-C_8-cycloalkyl-C_1-C_6-alkyl, ar-C_1-C_6-alkoxycarbonyl, C_1-C_6-alkoxycarbonyl, and C_1-C_6-alkanoyl, or

two substituents such that the two substituents, together with the amino-C_1-C_6-alkyl nitrogen, form a 5- to 8-membered heterocyclo or heteroaryl ring;

m is zero, 1, or 2;

n is zero, 1, or 2;

p is zero, 1, or 2;

the sum of m + n + p = 2;

one of X, Y, and Z is O, and the remaining two of X, Y, and Z are CR^8R^9 and $CR^{10}R^{11}$;

as to R^8:

R^8 is selected from the group consisting of hydrido, hydroxy, C_1-C_6-alkyl, C_1-C_6-alkanoyl, aroyl, aryl, ar-C_1-C_6-alkyl, heteroaryl, heteroar-C_1-C_6-alkyl, C_2-C_6-alkynyl, C_2-C_6-alkenyl, thiol-C_1-C_6-alkyl, C_1-C_6-alkylthio-C_1-C_6-alkyl, cycloalkyl,

cycloalkyl-C_1-C_6-alkyl, heterocyclo-C_1-C_6-alkyl, C_1-C_6-alkoxy-C_1-C_6-alkyl, aralkoxy-C_1-C_6-alkyl, C_1-C_6-alkoxy-C_1-C_6-alkoxy-C_1-C_6-alkyl, hydroxy-C_1-C_6-alkyl, hydroxycarbonyl-C_1-C_6-alkyl, hydroxycarbonylar-C_1-C_6-alkyl, aminocarbonyl-C_1-C_6-alkyl, aryloxy-C_1-C_6-alkyl, heteroaryloxy-C_1-C_6-alkyl, arylthio-C_1-C_6-alkyl, heteroarylthio-C_1-C_6-alkyl, a sulfoxide of any of said thio substituents, a sulfone of any said thio substituents, perfluoro-C_1-C_6-alkyl, trifluoromethyl-C_1-C_6-alkyl, halo-C_1-C_6-alkyl, alkoxycarbonylamino-C_1-C_6-alkyl, and amino-C_1-C_6-alkyl, wherein:

the aminoalkyl nitrogen optionally is substituted with up to two substituents independently selected from the group consisting of C_1-C_6-alkyl, ar-C_1-C_6-alkyl, cycloalkyl, and C_1-C_6-alkanoyl,

R^8 and R^9, together with the carbon to which they are bonded, form a carbonyl group, or

R^8 and R^9 or R^8 and R^{10}, together with the atom(s) to which they are bonded, form a 5- to 8-membered carbocyclic ring or a 5- to 8-membered heterocyclo or heteroaryl ring comprising one or two heteroatoms independently selected from the group consisting of nitrogen, oxygen, and sulfur;

as to R^9:

R^9 is selected from the group consisting of hydrido, hydroxy, C_1-C_6-alkyl, C_1-C_6-alkanoyl, aroyl, aryl, ar-C_1-C_6-alkyl, heteroaryl, heteroar-C_1-C_6-alkyl, C_2-C_6-alkynyl, C_2-C_6-alkenyl, thiol-C_1-C_6-alkyl, C_1-C_6-alkylthio-C_1-C_6-alkyl, cycloalkyl, cycloalkyl-C_1-C_6-alkyl, heterocyclo-C_1-C_6-alkyl, C_1-C_6-alkoxy-C_1-C_6-alkyl, aralkoxy-C_1-C_6-alkyl, C_1-C_6-alkoxy-C_1-C_6-alkoxy-C_1-C_6-alkyl, hydroxy-C_1-C_6-alkyl, hydroxycarbonyl-C_1-C_6-alkyl, hydroxycarbonylar-C_1-C_6-alkyl, aminocarbonyl-C_1-C_6-alkyl, aryloxy-C_1-C_6-alkyl, heteroaryloxy-C_1-C_6-alkyl, arylthio-C_1-C_6-alkyl, heteroarylthio-C_1-C_6-alkyl, a sulfoxide of any of said thio substituents, a sulfone of any said thio substituents, perfluoro-C_1-C_6-alkyl, trifluoromethyl-C_1-C_6-alkyl, halo-C_1-C_6-alkyl, alkoxycarbonylamino-C_1-C_6-alkyl, and amino-C_1-C_6-alkyl, wherein:

the aminoalkyl nitrogen optionally is substituted with up to two substituents independently selected from the group consisting of C_1-C_6-alkyl, ar-C_1-C_6-alkyl, cycloalkyl, and C_1-C_6-alkanoyl,

R^9 and R^8, together with the carbon to which they are bonded, form a carbonyl group, a 5- to 8-membered carbocyclic ring, or a 5- to 8-membered heterocyclo or heteroaryl ring comprising one or two heteroatoms independently selected from the group consisting of nitrogen, oxygen, and sulfur;

as to R^{10}:

R^{10} is selected from the group consisting of hydrido, hydroxy, C_1-C_6-alkyl, C_1-C_6-alkanoyl, aroyl, aryl, ar-C_1-C_6-alkyl, heteroaryl, heteroar-C_1-C_6-alkyl, C_2-C_6-alkynyl, C_2-C_6-alkenyl, thiol-C_1-C_6-alkyl, C_1-C_6-alkylthio-C_1-C_6-alkyl, cycloalkyl, cycloalkyl-C_1-C_6-alkyl, heterocyclo-C_1-C_6-alkyl, C_1-C_6-alkoxy-C_1-C_6-alkyl, aralkoxy-C_1-C_6-alkyl, C_1-C_6-alkoxy-C_1-C_6-alkoxy-C_1-C_6-alkyl, hydroxy-C_1-C_6-alkyl, hydroxycarbonyl-C_1-C_6-alkyl, hydroxycarbonylar-C_1-C_6-alkyl, aminocarbonyl-C_1-C_6-alkyl, aryloxy-C_1-C_6-alkyl, heteroaryloxy-C_1-C_6-alkyl, arylthio-C_1-C_6-alkyl, heteroarylthio-C_1-C_6-alkyl, a sulfoxide of any of said thio substituents, a sulfone of any said thio substituents, perfluoro-C_1-C_6-alkyl, trifluoromethyl-C_1-C_6-alkyl, halo-C_1-C_6-alkyl, alkoxycarbonylamino-C_1-C_6-alkyl, and amino-C_1-C_6-alkyl, wherein:

the aminoalkyl nitrogen optionally is substituted with up to two substituents independently selected from the group consisting of C_1-C_6-alkyl, ar-C_1-C_6-alkyl, cycloalkyl, and C_1-C_6-alkanoyl,

R^{10} and R^{11}, together with the carbon to which they are bonded, form a carbonyl group, or

R^{10} and R^8 or R^{10} and R^{11}, together with the atom(s) to which they are bonded, form a 5- to 8-membered carbocyclic ring or a 5- to 8-membered heterocyclo or heteroaryl ring comprising one or two heteroatoms independently selected from the group consisting of nitrogen, oxygen, and sulfur;

as to R^{11}:

R^{11} is selected from the group consisting of hydrido, hydroxy, C_1-C_6-alkyl, C_1-C_6-alkanoyl, aroyl, aryl, ar-C_1-C_6-alkyl, heteroaryl, heteroar-C_1-C_6-alkyl, C_2-C_6-alkynyl, C_2-C_6-alkenyl, thiol-C_1-C_6-alkyl, C_1-C_6-alkylthio-C_1-C_6-alkyl, cycloalkyl, cycloalkyl-C_1-C_6-alkyl, heterocyclo-C_1-C_6-alkyl, C_1-C_6-alkoxy-C_1-C_6-alkyl, aralkoxy-C_1-C_6-alkyl, C_1-C_6-alkoxy-C_1-C_6-alkoxy-C_1-C_6-alkyl, hydroxy-C_1-C_6-alkyl, hydroxycarbonyl-C_1-C_6-alkyl, hydroxycarbonylar-C_1-C_6-alkyl, aminocarbonyl-C_1-C_6-alkyl, aryloxy-C_1-C_6-alkyl, heteroaryloxy-C_1-C_6-alkyl, arylthio-C_1-C_6-alkyl, heteroarylthio-C_1-C_6-alkyl, a sulfoxide of any of said thio substituents, a sulfone of any said thio substituents, perfluoro-C_1-C_6-alkyl, trifluoromethyl-C_1-C_6-alkyl, halo-C_1-C_6-alkyl, alkoxycarbonylamino-C_1-C_6-alkyl, and amino-C_1-C_6-alkyl, wherein:

the aminoalkyl nitrogen optionally is substituted with up to two substituents independently selected from the group consisting of C_1-C_6-alkyl, ar-C_1-C_6-alkyl, cycloalkyl, and C_1-C_6-alkanoyl,

R^{11} and R^{10}, together with the carbon to which they are bonded, form a carbonyl group, a 5- to 8-membered carbocyclic ring, or a 5- to 8-membered heterocyclo or heteroaryl ring comprising one or two heteroatoms independently selected from the group consisting of nitrogen, oxygen, and sulfur;

only one of R^8 and R^9 or R^{10} and R^{11} is hydroxy; and

R^3 is substituted aryl or substituted heteroaryl, wherein:

the substituent on the aryl or heteroaryl is selected from the group consisting of optionally substituted cycloalkyl, heterocyclo, aryl, heteroaryl, aralkyl, heteroaralkyl, aralkoxy, heteroaralkoxy, aralkoxyalkyl, aryloxyalkyl, aralkanoylalkyl, arylcarbonylalkyl, aralkylaryl, aryloxyalkylaryl, aralkoxyaryl, arylazoaryl, arylhydrazinoaryl, alkylthioaryl, arylthioalkyl, alkylthioaralkyl, aralkylthioalkyl, aralkylthioaryl, a sulfoxide of any of the thio substituents, a sulfone of any of the thio substituents, and a fused ring structure comprising at least two 5- to 6-membered rings

independently selected from the group consisting of aryl, heteroaryl, cycloalkyl, and heterocyclo, wherein:

each optional substituent of any such group is independently selected from the group consisting of cyano, perfluoroalkyl, trifluoromethoxy, trifluoromethylthio, haloalkyl, trifluoromethylalkyl, aralkoxycarbonyl, aryloxycarbonyl, hydroxy, halo, alkyl, alkoxy, nitro, thiol, hydroxycarbonyl, aryloxy, arylthio, aralkyl, aryl, arylcarbonylamino, heteroaryloxy, heteroarylthio, heteroaralkyl, cycloalkyl, heterocyclooxy, heterocyclothio, heterocycloamino, cycloalkyloxy, cycloalkylthio, heteroaralkoxy, heteroaralkylthio, aralkoxy, aralkylthio, aralkylamino, heterocyclo, heteroaryl, arylazo, hydroxycarbonylalkoxy, alkoxycarbonylalkoxy, alkanoyl, arylcarbonyl, aralkanoyl, alkanoyloxy, aralkanoyloxy, hydroxyalkyl, hydroxyalkoxy, alkylthio, alkoxyalkylthio, alkoxycarbonyl, aryloxyalkoxyaryl, arylthioalkylthioaryl, aryloxyalkylthioaryl, arylthioalkoxyaryl, hydroxycarbonylalkoxy, hydroxycarbonylalkylthio, alkoxycarbonylalkoxy, alkoxycarbonylalkylthio, amino, carbonylamino, and aminoalkyl, wherein:

the amino nitrogen optionally is substituted with:

up to two substituents independently selected from the group consisting of alkyl, aryl, heteroaryl, aralkyl, cycloalkyl, aralkoxycarbonyl, alkoxycarbonyl, arylcarbonyl, aralkanoyl, heteroarylcarbonyl, heteroaralkanoyl, and alkanoyl, or

two substituents such that the two substituents, together with the amino nitrogen, form a 5- to 8-membered heterocyclo or heteroaryl ring that optionally:

comprises up to two additional heteroatoms independently selected from the group consisting of nitrogen, oxygen and sulfur, and

is substituted with up to two substituents independently selected from the group consisting of aryl, alkyl, heteroaryl, aralkyl, heteroaralkyl, hydroxy, alkoxy, alkanoyl, cycloalkyl, heterocyclo, alkoxycarbonyl,

hydroxyalkyl, trifluoromethyl, benzofused heterocyclo, hydroxyalkoxyalkyl, aralkoxycarbonyl, hydroxycarbonyl, aryloxycarbonyl, benzofused heterocycloalkoxy, benzofused cycloalkylcarbonyl, heterocyclo-alkylcarbonyl, and cycloalkylcarbonyl,

the carbonylamino nitrogen optionally is:

the reacted amine of an amino acid,

substituted with up to two substituents independently selected from the group consisting of alkyl, hydroxyalkyl, hydroxyheteroaralkyl, cycloalkyl, aralkyl, trifluoromethylalkyl, heterocyclo, benzofused heterocyclo, benzofused cycloalkyl, and N,N-dialkylsubstituted alkylamino-alkyl, or

substituted with two substituents such that the two substituents, together with the carbonylamino nitrogen, form a 5- to 8-membered heterocyclo, heteroaryl, or benzofused heterocyclo, wherein:

the heterocyclo, heteroaryl, or benzofused heterocyclo optionally is substituted with up to two substituents independently selected from the group consisting of alkyl, alkoxycarbonyl, nitro, heterocyclo, hydroxy, hydroxycarbonyl, aryl, aralkyl, heteroaralkyl, and amino, wherein the amino nitrogen optionally is substituted with:

up to two substituents independently selected from the group consisting of alkyl, aryl, and heteroaryl, or

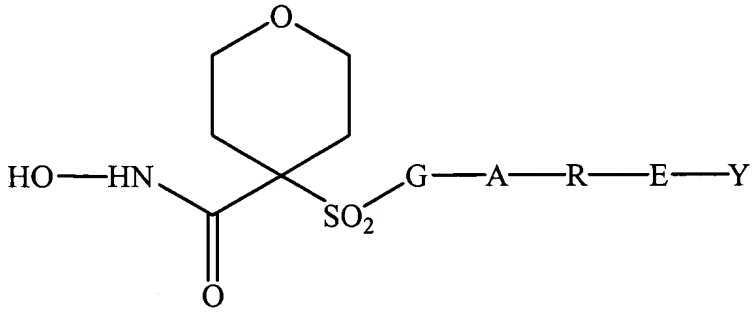
two substituents such that the two substituents, together with the amino nitrogen, form a 5- to 8-membered heterocyclo or heteroaryl ring;

the aminoalkyl nitrogen optionally is substituted with:

up to two substituents independently selected from the group consisting of alkyl, aryl, aralkyl, cycloalkyl, aralkoxycarbonyl, alkoxycarbonyl, and alkanoyl, or

two substituents such that the two substituents, together with the aminoalkyl nitrogen, form a 5- to 8 membered heterocyclo or heteroaryl ring.

159. **(new)** A compound or salt according to claim 158, wherein the compound corresponds in structure to the formula below:

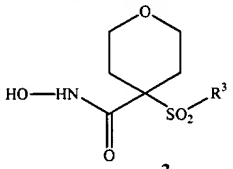
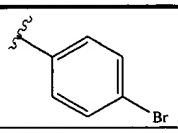
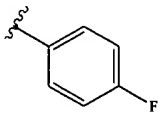
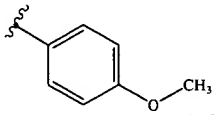
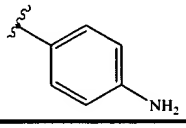


160. **(new)** The compound or salt according to claim 158, wherein the salt is a pharmaceutically acceptable salt.

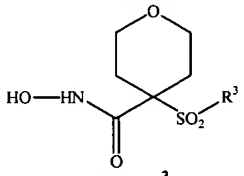
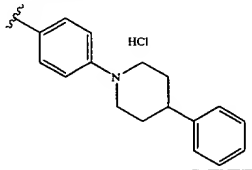
161. **(new)** A pharmaceutical composition, wherein the composition comprises a compound or pharmaceutically acceptable salt according to claim 160 dissolved or dispersed in a pharmaceutically acceptable carrier.

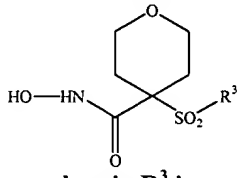
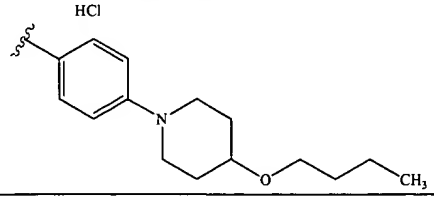
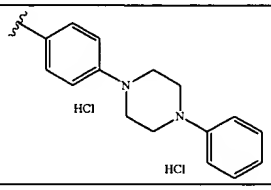
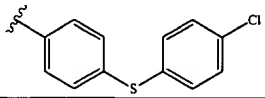
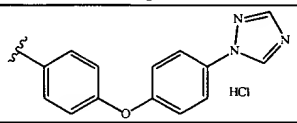
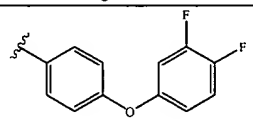
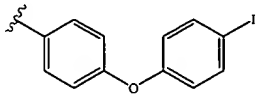
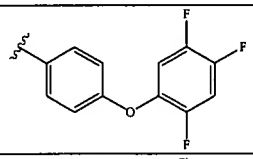
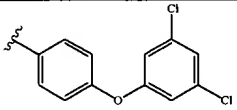
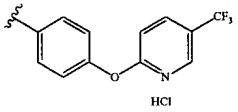
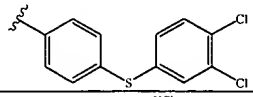
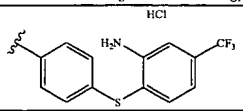
Appendix B
Comparison Between Tetrahydropyranyl Compounds and Salts Having a Single-Ring Substituent on the Sulfonyl and Tetrahydropyranyl Compounds and Salts Having a Multi-Ring Substituent on the Sulfonyl

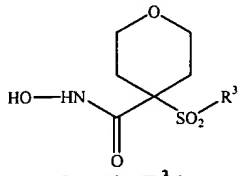
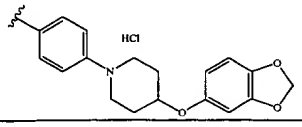
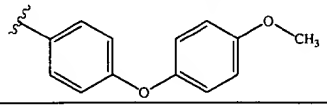
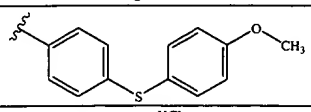
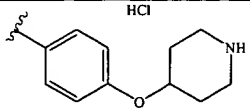
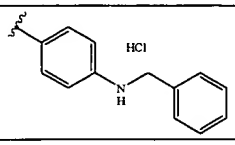
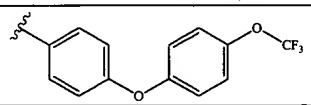
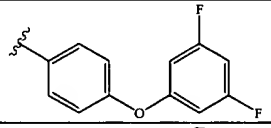
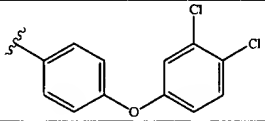
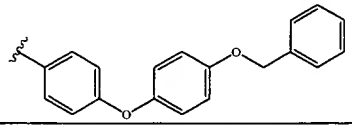
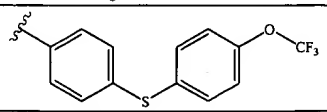
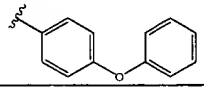
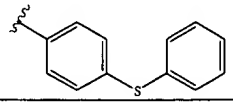
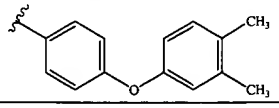
Data for Compounds and Salts Having a Single-Ring Substituent on the Sulfonyl

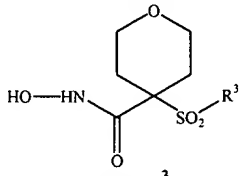
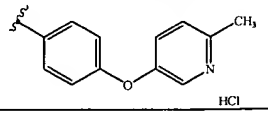
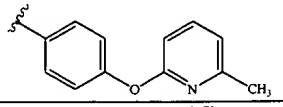
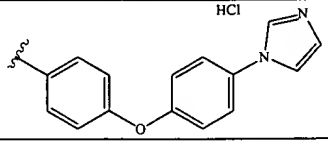
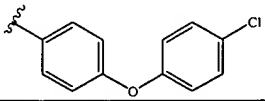
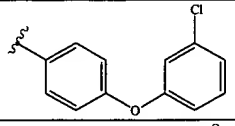
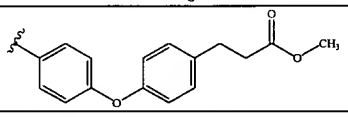
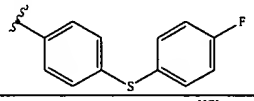
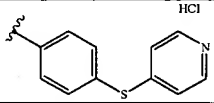
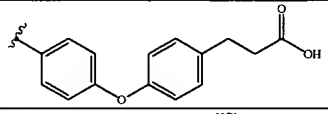
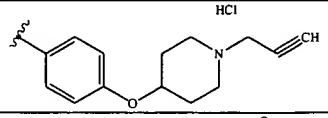
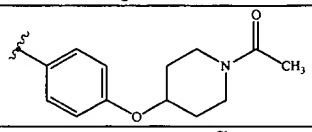
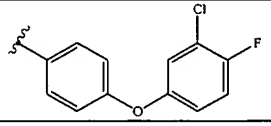
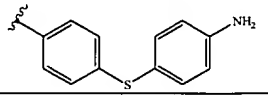
Source of Data	Structure  wherein R^3 is:	MMP-1 IC_{50}	MMP-13 IC_{50}	Selectivity MMP-1/ MMP-13
Dr. McDonald's Declaration		200	7.0	28.6
Example 66 in Applicants' Specification (also see Dr. McDonald's Declaration)		1600	268	5.97
Dr. McDonald's Declaration		1000	23.0	43.5
Dr. McDonald's Declaration		8000	30	267

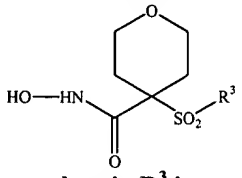
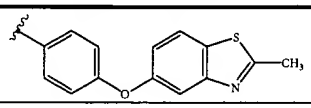
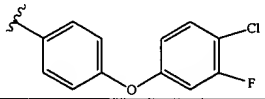
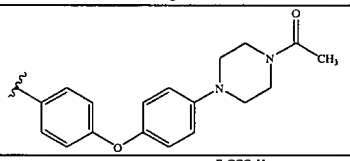
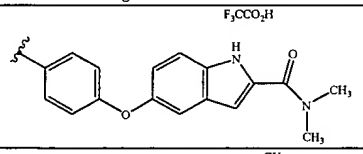
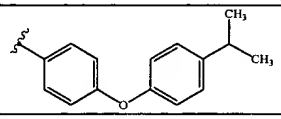
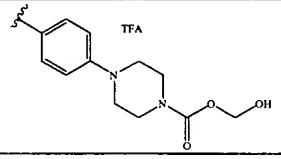
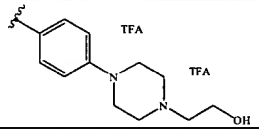
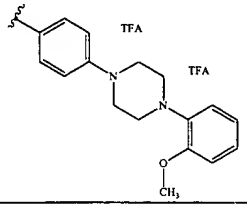
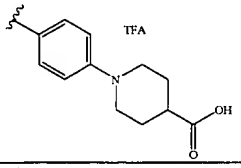
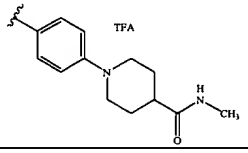
Data for Compounds and Salts Having a Multi-Ring Substituent on the Sulfonyl

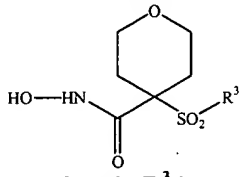
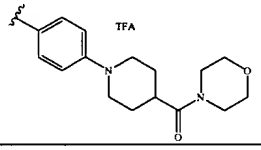
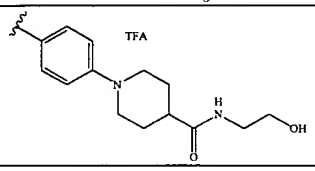
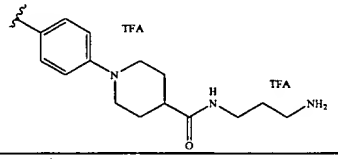
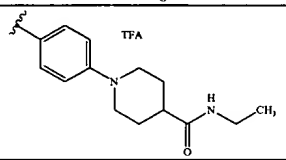
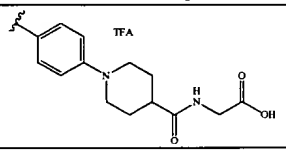
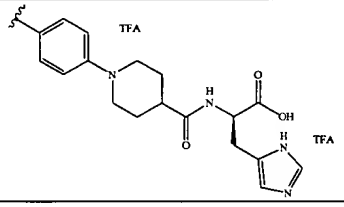
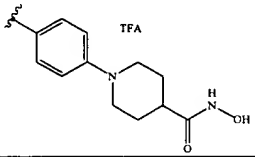
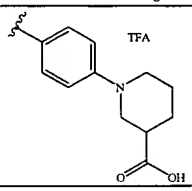
Example Number	Structure  wherein R^3 is:	MMP-1 IC_{50}	MMP-13 IC_{50}	Selectivity MMP-1/ MMP-13
11		>10000	6	>1670

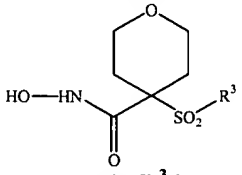
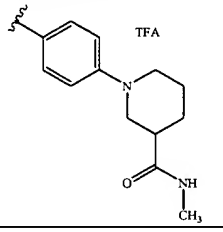
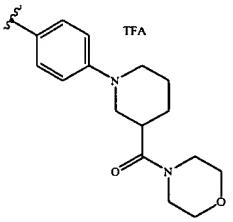
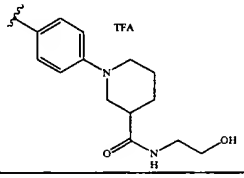
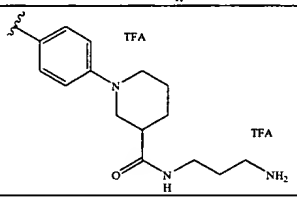
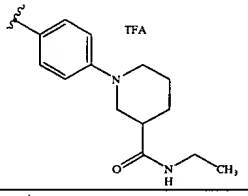
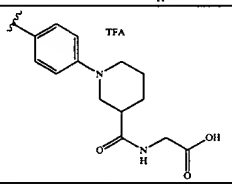
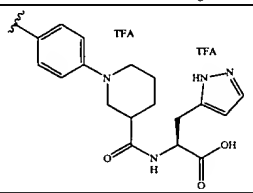
Example Number	Structure  wherein R^3 is:	MMP-1 IC_{50}	MMP-13 IC_{50}	Selectivity MMP-1/ MMP-13
16		>10000	2.4	>4170
20		10000	1.7	5880
25		>10000	3	>3330
26		7700	0.5	15400
56 (see also Dr. McDonald's Declaration)		1200	0.3	4000
57 (see also Dr. McDonald's Declaration)		1500	0.15	10000
58 (see also Dr. McDonald's Declaration)		1200	0.2	6000
59 (see also Dr. McDonald's Declaration)		>10000	30	>333
59(b) (see also Dr. McDonald's Declaration)		>10000	180	>55.6
60		>10000	147	68.0
61		>10000	2000	5

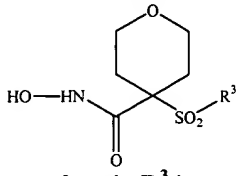
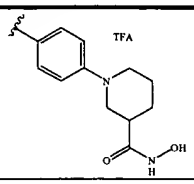
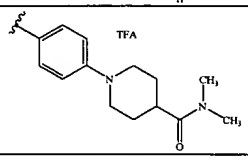
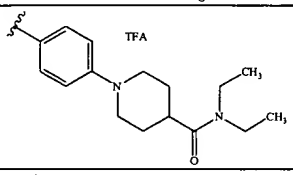
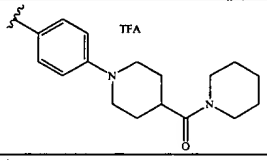
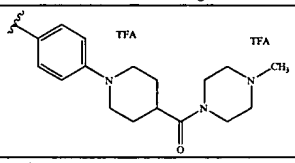
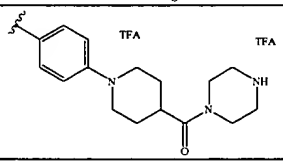
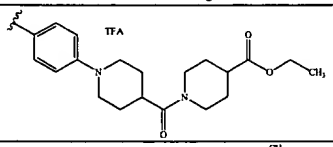
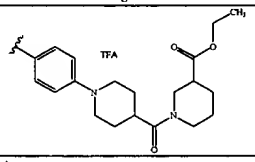
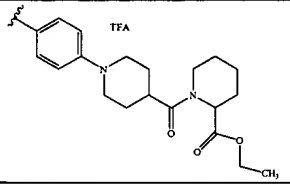
Example Number	Structure  wherein R^3 is:	MMP-1 IC_{50}	MMP-13 IC_{50}	Selectivity MMP-1/ MMP-13
63		>10000	1.5	6670
64		1470	0.15	2940
65		8000	0.7	11400
67 (see also Dr. McDonald's Declaration)		>10000	6000	1.67
68		>10000	6	>1670
69		1140	<0.1	>11400
70		1500	0.8	1880
71		3600	0.8	4500
72		2100	0.3	7000
73		1140	<0.1	>11400
94		268	<0.1	>2680
95		>10000	0.5	>20000
96		5000	0.3	16700

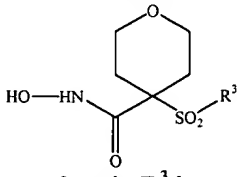
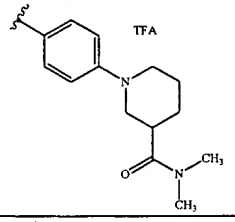
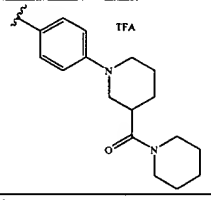
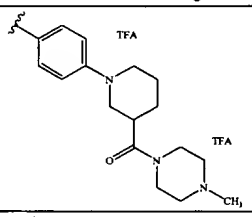
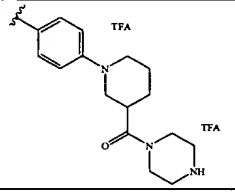
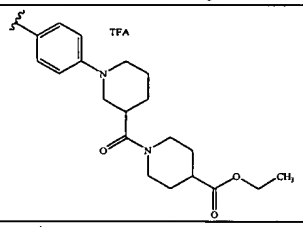
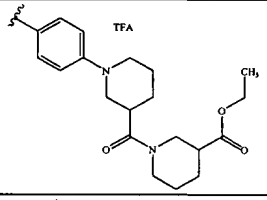
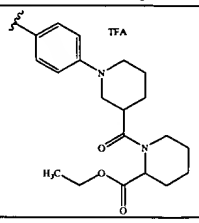
Example Number	Structure  wherein R^3 is:	MMP-1 IC_{50}	MMP-13 IC_{50}	Selectivity MMP-1/ MMP-13
97		4000	16.7	240
98		>10000	23.4	427
99		>10000	1	>10000
100		435	0.15	2900
101		1800	0.45	4000
102		2000	0.2	10000
103		>10000	0.7	>14300
104		>10000	0.65	>15400
105		>10000	0.85	>11800
106		>10000	12.1	826
107		>10000	6	1670
108		2000	0.4	5000
120		4000	0.4	10000

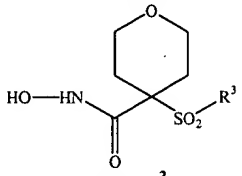
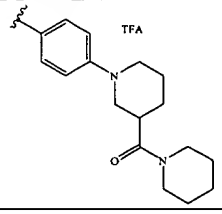
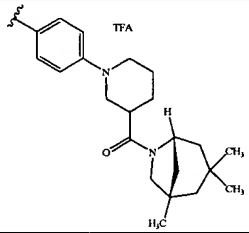
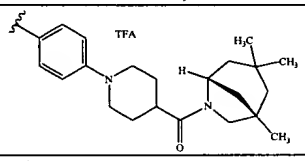
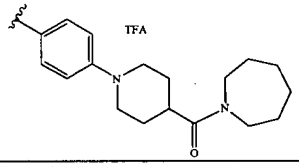
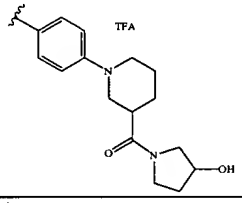
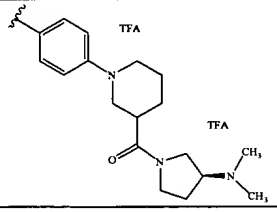
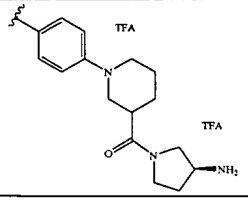
Example Number	Structure  wherein R^3 is:	MMP-1 IC_{50}	MMP-13 IC_{50}	Selectivity MMP-1/ MMP-13
121		1200	0.2	6000
122		600	0.15	4000
123		3600	1.8	2000
124		1000	1.1	909
125		>10000	0.5	>20000
126		8000	10	800
127		>10000	40	>250
128		>10000	20	>500
129		>10000	1000	>10
130		>10000	45.9	>218

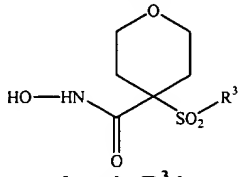
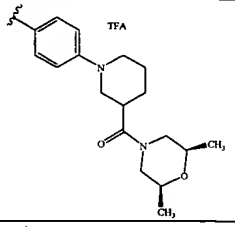
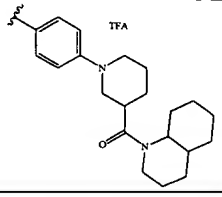
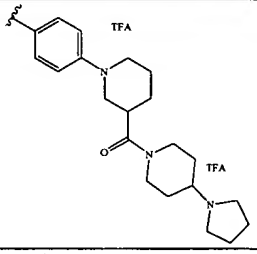
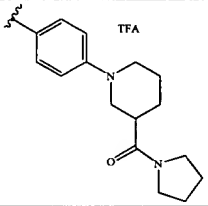
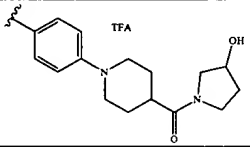
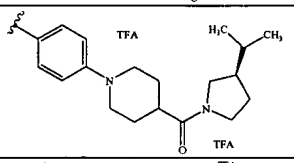
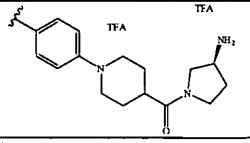
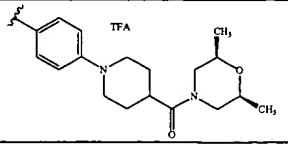
Example Number	Structure  wherein R^3 is:	MMP-1 IC_{50}	MMP-13 IC_{50}	Selectivity MMP-1/ MMP-13
131		>10000	10	>1000
132		>10000		
133		>10000	27	>370
134		9000	4	2250
135		>10000	65	>154
136		>10000	40	>250
137		>10000	34.7	>288
138		>10000	>100	100

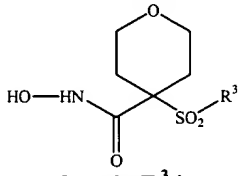
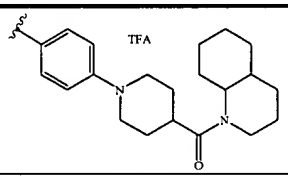
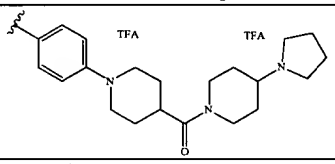
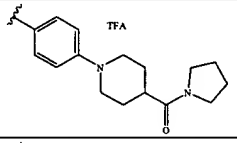
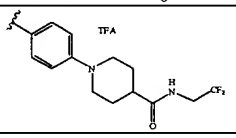
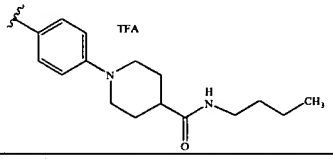
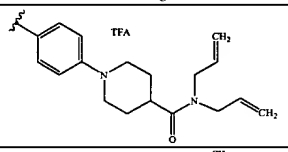
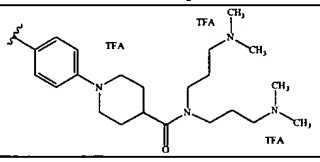
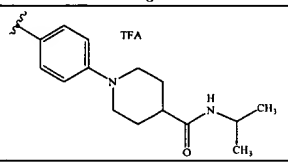
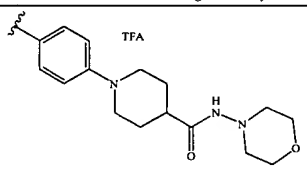
Example Number	Structure  wherein R^3 is:	MMP-1 IC_{50}	MMP-13 IC_{50}	Selectivity MMP-1/ MMP-13
139		>10000	25.4	>394
140		>10000	60	>167
141		>10000	>100	100
142		>10000	70	>143
143		>10000	23.9	>418
144		>10000	30.7	>326
145		>10000	>100	100

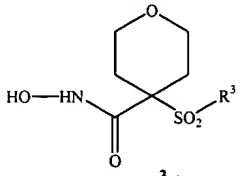
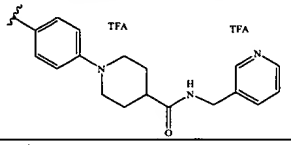
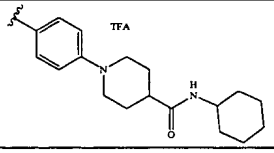
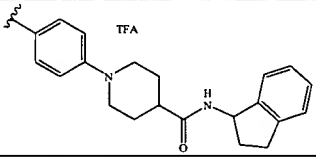
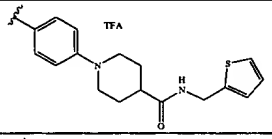
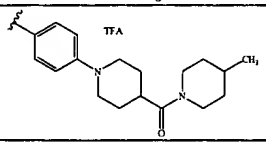
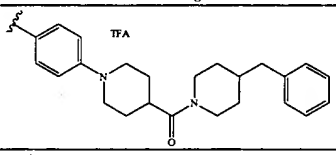
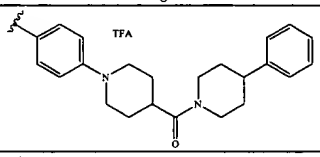
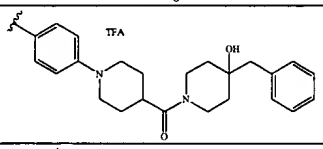
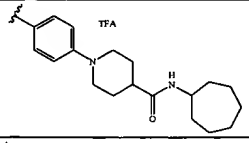
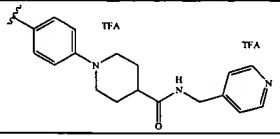
Example Number	Structure  wherein R^3 is:	MMP-1 IC_{50}	MMP-13 IC_{50}	Selectivity MMP-1/ MMP-13
146		>10000	32.6	>307
147		>10000	31	>322
148		>10000	31	>322
149		>10000	15.5	>645
150		>10000	14.5	>690
151		>10000	35	>286
152		>10000	16.5	>606
153		>10000	13.5	>741
154		>10000	27	>370

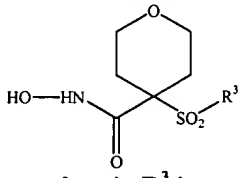
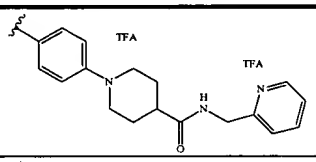
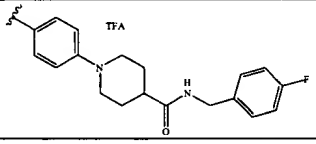
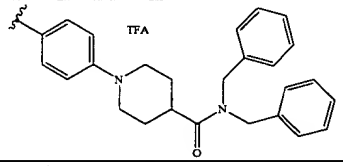
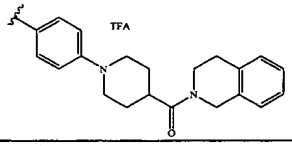
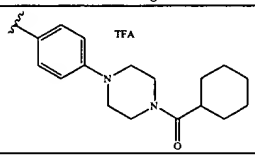
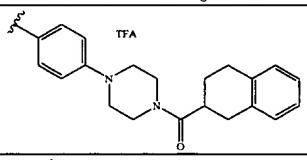
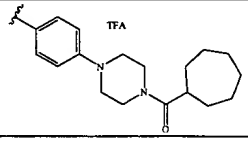
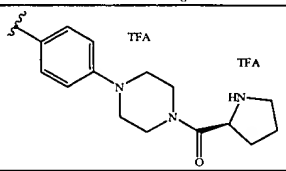
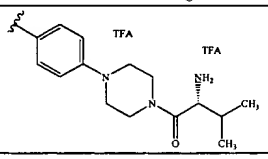
Example Number	Structure  wherein R^3 is:	MMP-1 IC_{50}	MMP-13 IC_{50}	Selectivity MMP-1/ MMP-13
155		>10000	>100	100
156		>10000	27.8	>360
157		>10000	90	>111
158		>10000	80	>125
159		>10000	15.6	>641
160		>10000	33.7	>297
161		>10000	>100	100

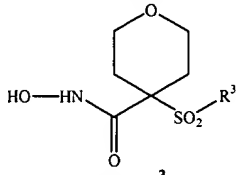
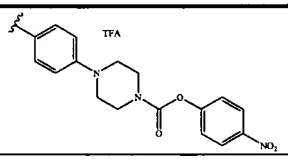
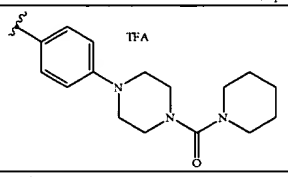
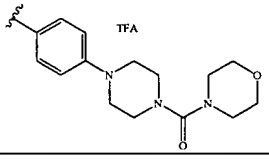
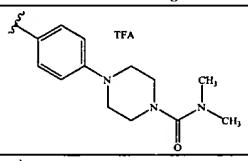
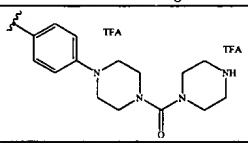
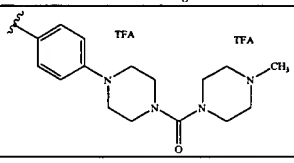
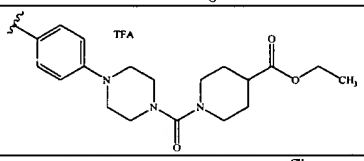
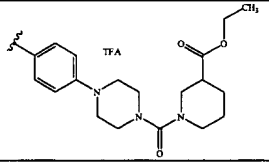
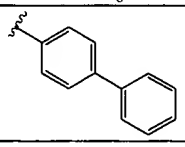
Example Number	Structure  wherein R^3 is:	MMP-1 IC_{50}	MMP-13 IC_{50}	Selectivity MMP-1/ MMP-13
162		>10000	>100	100
163		>10000	77.4	>129
164		>10000	20	>500
165		>10000	13.6	>735
166		>10000	>100	100
167		>10000	>100	100
168		>10000	>100	100

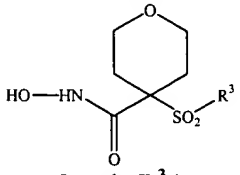
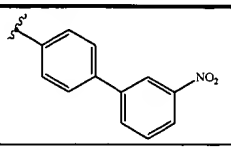
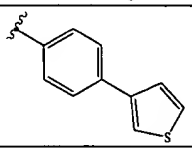
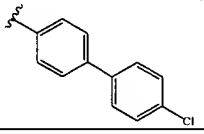
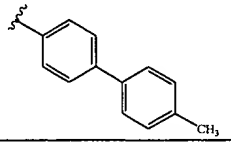
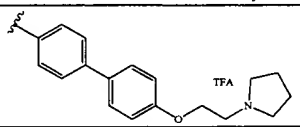
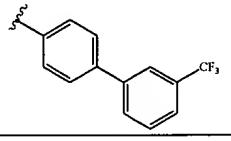
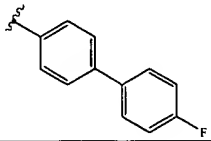
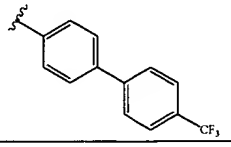
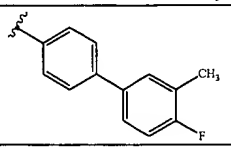
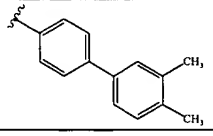
Example Number	Structure  wherein R^3 is:	MMP-1 IC_{50}	MMP-13 IC_{50}	Selectivity MMP-1/ MMP-13
169		10000	>100	<100
170		10000	>100	<100
171		>10000	>100	100
172		>10000	>100	100
173		>10000	>100	100
174		8000	>100	<80
175		10000	>100	<100
176		>10000	25	>400

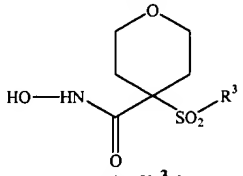
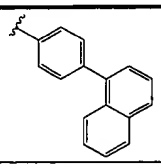
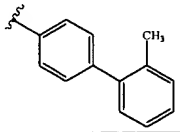
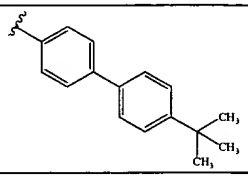
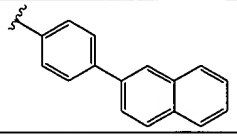
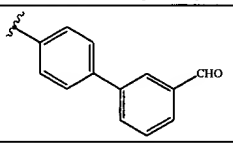
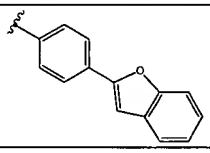
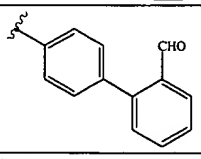
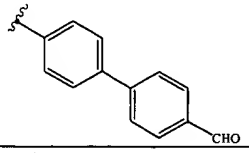
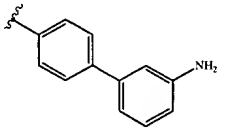
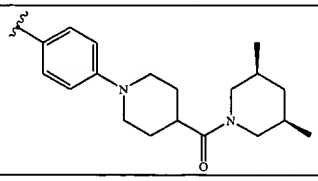
Example Number	Structure  wherein R^3 is:	MMP-1 IC_{50}	MMP-13 IC_{50}	Selectivity MMP-1/ MMP-13
177		>10000	21	>476
178		>10000	>100	100
179		>10000	100	>100
180		5000	4	1250
181		10000	6.1	1640
182		>10000	4	>2500
183		>10000	40	>250
184		>10000	7	>1430
185		>10000	17.5	>571

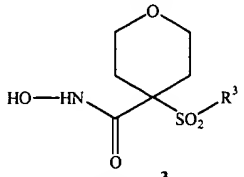
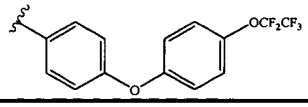
Example Number	Structure  wherein R^3 is:	MMP-1 IC_{50}	MMP-13 IC_{50}	Selectivity MMP-1/ MMP-13
186		>10000	10	>1000
187		>10000	12.1	>826
188		>10000	9.4	>1060
189		3700	8	462
190		>10000	10.6	>943
191		>10000	4	>2500
192		>10000	10	>1000
193		>10000	6	>1670
194		10000	8	1250
195		10000	14.5	690

Example Number	Structure  wherein R^3 is:	MMP-1 IC_{50}	MMP-13 IC_{50}	Selectivity MMP-1/ MMP-13
196		>10000	25	>400
197		7000	8	875
198		>10000	14.5	>690
199		>10000	1.4	>7140
200		>10000	17.5	>571
201		>10000	13.6	>735
202		>10000	9.15	>1090
203		8500	30	283
204		>10000	27.1	>369

Example Number	Structure  wherein R^3 is:	MMP-1 IC_{50}	MMP-13 IC_{50}	Selectivity MMP-1/ MMP-13
205		7300	2	3650
206		>10000	20	>500
207		>10000	28	>357
208		>10000	27	>370
209		>10000	20	>500
210		>10000	20	>500
211		>10000	24	>417
212		>10000	20	>500
213		310	<1.0	>310

Example Number	Structure  wherein R^3 is:	MMP-1 IC_{50}	MMP-13 IC_{50}	Selectivity MMP-1/ MMP-13
214		1100	<1.0	>1100
215		250	<1.0	>250
216		1000	<1. 0	>1000
217		600	<1.0	>600
218		>10000	<1.0	>10000
219		>10000	<1.0	>10000
220		145	<1.0	>145
221		1600	<1.0	>1600
222		100	<1.0	>100
223		1100	<1.0	>1100

Example Number	Structure  wherein R^3 is:	MMP-1 IC_{50}	MMP-13 IC_{50}	Selectivity MMP-1/ MMP-13
224		>10000	16.7	>599
225		>10000	70	>143
226		>10000	6	>1670
227		>10000	<1	>10000
228		600	<1.0	>600
229		>10000	<1	>10000
230		>10000	>100	100
231		650	<1.0	>650
232		<100	<1.0	100
498		>10000	10	>1000

Example Number	Structure  wherein R^3 is:	MMP-1 IC_{50}	MMP-13 IC_{50}	Selectivity MMP-1/ MMP-13
667		4500	<0.1	>45000

Attorney Docket No. 3124/4/US
HDP Docket No. 6794-000021/US

CERTIFICATE OF MAILING

I certify that this **Amendment B** is being deposited with the United States Postal Service as first class mail in an envelope addressed to: **Assistant Commissioner for Patents, Washington, D.C. 20231 on November 5, 2001**.

Lana B. Ekiss

DMG/LE